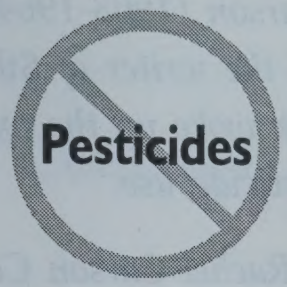
RESOURCE MANUAL ON HAZARDS OF Pesticides

Some Less Known Facts on our Registered Pesticides

Navdanya



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Dedicated to the memory of Rachel Carson (1908-1964), the distinguished marine biologist and the writer of Silent Spring in 1962, whose pioneering work woke up the world to the serious risks and dangers of pesticide use.

Following her death in 1964, a Trust, Rachel Carson Council Inc. has been created in 1965 at 8940 Jones Mill Road, Chevy Chase Maryland USA 20815

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January 2004

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Published by
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New Delhi - 110 016 INDIA
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Printed by
Systems Vision, A-199 Okhla Phase-I
New Delhi - 110 020

Contents

Acknowledgements

- Dr. Shirley Ann Briggs and the staff of Rachel Carson Council Inc. Chevy Chase, Maryland 20815, USA: Basic Guide to Pesticides - their characteristics and hazards, 1993, Rachel Carson Council Inc. Published by Taylor and Francis, Washington D.C. USA. Their work is presented on pages 1-37.
- Dr. Caroline Cox and the staff of North-West Coalition for Alternatives to Pesticides (NCAP) Eugene Oregon, USA and its Director Dr. Norma Grier for their work reproduced on pages 38-74. This work has been taken from the various issues of Global Pesticide Campaigner published by the Pesticide Action Network, North America, San Francisco USA by its Director Monica Moore and staff.
- Facts Sheets on individual pesticides reproduced on pages 75-111 from various issues of Pesticides News edited by David Buffin and its staff under Pesticide Action Network-UK, London UK under its present Director Barbara Dinharn and Guest Editor, Dorothy Myers, Pesticide News.
- WHO-IPCs, Geneva, Guidelines to Classification 1998-99.
- Dr. D. Kanungo, Directorate of Plant Protection, Quarantine, Storage, Ministry of Agriculture, Govt. of India, Faridabad, Haryana.
- Dr. SP Singh, Head, Project Directorate of Biological Control (ICAR) Bangalore.
- Special thanks are due to Dr. Poonam Pande and Dr. Radha Holla Bhar of Navdanya for various inputs and support.
- Special thanks are due to Dr. Vandana Shiva Founder Director of Navdanya for providing inspiration, encouragement and support in her single minded pursuit of exposing the perils of pesticides, to the author, Dr. AT Dudani during his six month tenure as a Consultant with Navdanya/Research Foundation for Science, Technology and Ecology during the period 1 May 2002–31 October 2002.

Introduction

Pesticides have largely been in the top news largely when some mass poisoning and deaths take place as for instance in 1958 when 102 people died in Kerala/ Tamil Nadu. These followed consumption of food on board a ship from USA which got accidentally admixed with ethyl parathion. This led to setting up of the Shah Commission in 1958 leading to another Committee under late Prof Thacker in 1964 followed by the Insecticide Act in 1968. This resulted in creation of a sizeable infrastructure for registration of pesticides for their safety. This has grown and multiplied at Faridabad and New Delhi and elsewhere in the country with Laboratories set up for testing of pesticides for their adulteration to ensure their purity.

However the problem of poisonings both reported and largely unreported continues for a variety of reasons even though pesticide poisoning is now a notifiable event. Some recent cases of large scale poisoning were reported a few years back from Basti in UP with some 200 deaths and more recently from Warangal area of A.P and other cotton growing areas. claiming over 500 deaths. Some recent reports also claim deaths due to Endosulphan spraying in Kerala to save cashew nuts crops from pests.

Yet India continues to have one of the lowest reported poisonings and deaths from pesticides due largely on a non existing reporting system as required under the laws.

And yet the reports continue to trickle in. For instance a recent report from 10 Hospitals shows 1531 poisonings for 1999-2000. Of these 35% were amongst females. However this report creates the impression that bulk of the cases were due to intentional taking of pesticides obviously for suicide. On the other hand reports for three years1987-1989 show a somewhat different picture where the reports were the highest for Mahrashtra followed by Kerala, Punjab and Rajasthan. Interestingly of the 32 States and Union Territories there were no reports or nil reports from 23 of these States! These clearly show the rather unhappy state of reporting poisonings in the country.

According to the ICAR sources only 1% of pesticides actually reaches the target pests and the rest go to non-target sectors. It has also been estimated that despite heavy pesticide use pests are now causing damage to some 35% of the crops as against pre-pesticide era of 5-10% damage. There are estimated 5-10 million insect species in the eco system and only 0.03% of these cause damage direct or indirect to the crops. Incidentally as per official sources, pesticides are being used currently on about 25% of the farm land in the country. As per estimates while in 1920 there were some 40 damaging insects against paddy these had increased in 1992 to 200. For pulses it was 10 in 1920 and up to 240 in 1995. In case sugarcane the figure for 1920 was 20 and for 1992 this rose to 220 while for cotton these were 30 for 1920 and 150 for 1992 and for wheat these were 10 and 120 respectively.

To compound these issues the registration and use of pesticides goes on merrily. While for instance the registered pesticides in 1986 were 111 with a production of about 60,000 MT. In 1998 this figure stood at 148 and going up to 168 in 2001 and currently this has been raised to 177. The annual production has also touched an all time high of 91,000 MT (which covers both for agriculture and public health). The annual market value of pesticides is estimated at Rs.3500 crores with annual exports of around Rs 1200 crores to some 110 countries. And the poisonings and deaths continue unfettered even though grossly under reported.

Yet out of these 177 registered pesticides, there are only 2 Bio pesticides considered very safe- Neem and B.t. preparations.

This is not with standing the fact that the Indian scientists despite their many constraints have developed and brought out large number of bio pesticides to control a wide variety of common pests which damage a number of crops. Incidentally as per official sources, at present only about 25% of the farmland in the country is covered by chemical pesticides.

These are in the form of some 39 parasitoids, 22 predators, some 7 bacterial formulations, 6 viral preparations for control of a wide range of pests. This is in addition to 2 bio pesticides to control nematodes and several pheromones to lure pests. In addition some 67 Neem based preparations are already in the market. It is also common knowledge that pest attacks can be marginalised as was the case under indigenous and traditional system of farming all over the world using various cropping patterns to keep the pests away from causing any serious damage.

Unfortunately even though these bio control products have been developed by the Central and State Govt agencies and under commercial production by the small scale industry in the country, the necessary facilities and infrastructure and support for undertaking controlled trials seems to be weak or absent as our entire system is geared to use of chemical pesticides even though these are increasingly unpopular in the West where there is a strong movement towards organic farming.

It is therefore time that the public, the policy and decision makers take into account the serious consequences from use of pesticides to health of workers, the consumers, damage to the environment and use of high fossil fuel energy inputs needed for pesticide manufacture instead of repeating the oft repeated and now discarded bogey of starvation if the pesticide use was discontinued,

There is also a strong case for strengthening of R and D into development of bio pesticides including many time tested Plant pesticides and more importantly their use and trials under controlled conditions and popularisation amongst end users as has been done over the decades for promoting chemical pesticides.

Considering that despite these bottlenecks and the constraints the R and D scientists and the industry without any positive support from the Govt. are promoting and marketing many of these products and preparations is indeed a tribute both to our dedicated R and D scientists and the industry.

Considering the risks the pesticides pose to the population and the environment in general and since there is hardly any access to the user of any information on each of these pesticides which normally remain in the archives of the authorities , an attempt has been made to compile from the published data For this reliance has been placed largely on the data compiled by Dr. Shirley A Briggs of the Rachel Carson Council in her monumental, Basic Guide to Pesticides- Their characteristics and Hazards published by Taylor and Francis Ltd. of London and Washington DC in 1993 . These have been brought out on pages 1-37 covering almost all the pesticides that were accepted for use in the USA. These have been presented in a tabular form giving Common Trade and other chemical description. The table also states the class of chemical, the chief pesticide use and its status. The table also gives its persistence, effect on mammals, immediate (acute) and long term (chronic) toxicity, followed by description of adverse effects on other non- target species along with physical properties. Equally important is the information on contaminants in the pesticides arising from chemical manufacturing process, the transformation products, isomers and related information.

While the Manual has hundreds of pesticides covered, we have taken in our present publication details of some 100 such chemicals which are a part of the new list of Registered 177 Pesticides approved by the Govt. of India during 2002 a reference to which has already been made. We are in debt of gratitude to Dr Shirley A Briggs and her associates who spent years on this brilliant compilation. We are no doubt grateful to the present management of the Rachel Carson Council Inc, 8940 Jones Milp Road, Chevy Chase, Maryland 20815, USA email: rccouncil@aol.com who readily and graciously granted us permission for reproduction of this precious information. We therefore take this opportunity to honour late Rachel Carson of Silent Spring fame who brought to public notice the perils of pesticides way back in 1962 by dedicating this publication to her memory.

Since the professional, accurate information on pesticides is not only scarce but hard to collect and collate requiring not only dedication but also other inputs, we have incorporated some of the Fact Sheets on some of the pesticides published by Pesticide Action Network, San Francisco, California, USA (email: panna@panna.org)

in their Global Pesticide Campaigner issues and by the Pesticide Trust London (email: admin@pan-uk.org) in the various issues of Pesticide New pages 75-111. Both these are public interest groups dedicated to creating awareness to the true state of affairs and world wide data and experience gained and collected and collated by them. Our many thanks to both these organisations and to the distinguished Researcher Dr Ms.Caroline Cox of the Northwest Coalition for Alternatives to Pesticides. PO Box 1393 Eugene, Oregon USA who has contributed the Fact Sheets in the Global Pesticide Campaigner which we are reproducing in this publication pages 38-74.

List of 177 pesticides registered by the Govt. of India showing where possible the WHO Class is also provided alongwith a list of seven Restricted pesticides. A list of 24 banned pesticides is at A and B gives list of4 pesticide formulations banned and C gives list of three pesticides/ pesticide formulations banned for use but manufacture permitted for exports.

To highlight the dangers caused by pesticide poisonings, a chart of the Govt. of India is included for 1996-1999) to show the trends even though these are obviously totally under reported since most of the States fail to provide information or give Nil reports even though it has been made mandatory by the Govt. of India.

A Proforma for reporting cases of pesticides is also included which would help, hopefully to gather more information from our valued readers in this country for future compilation and use.

A chart showing the increase in resistance amongst pests since the chemical pesticide use started sometime during and after the World War II has also been included to highlight the pesticide treadmill we have got engulfed in from the time the pesticides have entered our lives even though alternatives were and are even today available which need to be developed now even more vigorously if we are to successfully overcome the situation we are in today (ICAR, New Delhi, PDBC Perspective Plan, Vision 2020).

An illustration showing the impact of pesticides on the human body and the system has also been provided to illustrate the dangers and how to ward these off, as a Guide to pesticide exposure for physicians (Pesticide News 31, March 1996, p.12).

Factsheets on Pesticides

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
acephate Orthene; Ortho 12420; Ortran *O,S*-dimethyl acetylphosphoramidothioate; *O,S*-dimethyl acetic phosphoramidothioate CAS # 30560-19-1	organo-phosphate	insecticide	non-pers (1)	oral: medium to high (2,3) dermal: ? inhalation: medium (1)	suspect carcinogen (4) suspect mutagen (4) fetotoxin (4) "some evidence of hormonal effects" (5)	immediate toxicity: birds: medium to high (6) fish: low (7) crustaceans: low (4) molluscs: medium (4) bees: high (13) plants: low; in plant tissue, metabolizes to acephate met (8-10) long-term toxicity: birds: may affect behavior and breeding success (11,12) water: "very soluble" slightly volatile
contaminant(s): **O,O,S-trimethyl phosphorothioate**				oral: high (1)	delayed toxicity (1)	
methylthioacetate				dermal: medium to high (1) inhalation: medium (1)	suspect mutagen (1) eye damage (1)	
transformation product(s): **acephate-met** (see acephate-met)						
acephate-met BAY 71628; Baythroid TM (with cyfluthrin); methamidophos; Monitor; Ortho 9006; SRA 5172; Tamaron; Tamaron (with parathion) *O,S*-dimethyl phosphoramidothioate CAS # 10265-92-6	organo-phosphate	insecticide restricted use: USA	non-pers (1)	oral: very high (2) dermal: very high (2) inhalation: high (3)	hair loss (8) decreased fertility (8)	immediate toxicity: birds: high (4) fish: low (5) bees: high (6) crustaceans: very high (7) water: "readily soluble" slightly volatile
alachlor Adeochlor; Bronco (with glyphosate); Bullet; Cannon; CP 50144; Lariat; Lasso (with atrazine); Lazo; Partner-Mon-9848; Pillarzo; Rambo (with atrazine) 2-chloro-2',6'-diethyl-*N*-(methoxymethyl)-acetanilide CAS # 15972-60-8	amide	herbicide banned in Canada, Sweden restricted use, USA	non-pers to mod-pers (1)	oral: medium (2) dermal: medium (1) inhalation: ?	carcinogen (3,4) suspect mutagen (5,6) eye damage: (3) kidney and liver damage (3)	immediate toxicity: birds: low to medium (1,7) fish: medium to high (1,8) bees: low to medium (9) water: soluble slightly volatile

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
allethrin Allethrin concentrate MGK; Alleviate; allycinerin; Exbiol; FDA 1446; FMC 249; Necarboxylic acid; Neo-Pynamin 5/1/30 (with phenothrin & piperonyl butoxide); NIA 249; OMS 468; pallethrine; Pesguard (with phenothrin & piperonyl butoxide); Pynamin; Pyrescel; Pyresin; Pyrocide; RU 28173; Sumithrin Plus (with phenothrin) (*RS*)-3-allyl-2-methyl-4-oxocyclopent-2-enyl (1*RS*)-*cis,trans*-chrysanthemate; (*RS*)-allethronyl (1*R,cis,trans*)chrysanthemate CAS # 584-79-2	pyrethroid	insecticide	?	oral: medium to high (1,2,3) dermal: low to medium (2,4) inhalation: medium to high (3)	suspect mutagen (5) suspect immunotoxin (6)	immediate toxicity: birds: low to medium (7,8) fish: low to very high (9,10) crustaceans: very high (10) aquatic insects: very high (10) volatile to highly volatile
isomer(s):						
***d-cis/trans*-allethrin** Pynamin Forte d-*cis/trans*-allethrin; (*RS*)-[1*R,cis,trans*]-chrysanthemate CAS # 42534-61-2	pyrethroid	insecticide	?	oral: high (1) dermal: ? inhalation: ?	?	immediate toxicity: fish: "very high" (2) combustible
esbiothrin allethrin stereoisomer; Detrans (with deltamethrin); K-O (with deltamethrin & piperonyl butoxide); OMS 3045; RU 27436 (*RS*)-allethronyl [1*R,trans*]-chrysanthemate	pyrethroid	insecticide	?	oral: high (1) dermal: "low" (2) inhalation: ?	?	
***S*-bioallethrin** Esbiol; esdepallethrin; OMS 3046; RU 16 121; RU 3054 d-allethronyl d-*trans*-allethrin; (+)-allethronyl (+)-*trans*-allethrin CAS # 28434-00-6	pyrethroid	insecticide	?	oral: medium to high (1,2) dermal: ? inhalation: medium to high (1)	?	immediate toxicity: birds: low (1) fish: medium to very high (1) water: medium volatile combustible
bioallethrin allethrin stereoisomer; depallethrin; Kefil (with permethrin & piperonyl butoxide); RU 11705; Vapona Flykiller (with permethrin & piperonyl butoxide) d-*trans*-allethrin; (+)-*trans*-allethrin; (*RS*)-allethronyl [1*R,trans*]-chrysanthemate CAS # 584-79-2	pyrethroid	insecticide	?	oral: medium to high (1,2) dermal: ? inhalation: medium (1)	suspect teratogen (3)	immediate toxicity: fish: very high (2) crustaceans: low (2) water: slightly soluble oil: slightly volatile to volatile combustible

Source: Rachel Carson Council Inc. USA

Factsheets on Pesticides

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
aluminum phosphide Celphos (India); Delicia (E. Germany); Phostoxin aluminum phosphide CAS # 1302-45-0	metal/ mineral aluminum	insecticide fumigant restricted use: USA	?	oral: very high (2) dermal: ? inhalation: ?	gastrointestinal damage (1) liver, heart, and kidney damage (1)	water: "slightly soluble"
transformation product(s):						
phosphine gas CAS # 7803-51-2				oral: very high (1) dermal: medium (1) inhalation: "poisonous" (2)		water: "slightly soluble" oil: "insoluble" combustible, "can ignite spontaneously in cold air; explosive"
atrazine AAtrex; Altacide Extra (with sodium chlorate); Atlazin (with amitrole); Atradex; Atradex 50; Atranex; Bellater (with cyanazine); Bicep (with metolachlor); Extrazine (with cyanazine); Fogard; Fogard L; Geigy 30,027; Gesaprim; Gesaprim D (with 2,4-D); Lasso (with alachlor); Primatol; Sutan+; Vectal; Vorox Granulat 371; Weedex A 2-chloro-4-ethylamino-6-isopropylamino-*s*-triazine CAS # 1912-24-9	triazine	herbicide restricted use, USA, 1990	mod-pers to pers (1,2)	oral: low to medium (3,4) dermal: medium (3) inhalation: "low" (4)	carcinogen (5,6) mutagen (7,8) immunotoxin (9) adrenal damage (10)	immediate toxicity: fish: low to high (4) crustaceans: low to medium (4) bees: medium (2) molluscs: high (1) aquatic insects: high to very high (13) long-term toxicity: soil invertebrates: may reduce populations (11) amphibians: may impair reproduction (13) water: slightly soluble slightly volatile
transformation product(s):						
N-nitrosoatrazine						
Bacillus thuringiensis (Berliner) B.T.	biological	insecticide	non-pers (1)	oral, dermal, inhalation: "non-toxic" (2,3)	?	?
varieties:						
Bacillus thuringiensis var. aizawei Certan *Bacillus thuringiensis*, variety *aizawei*		larvacide for wax moth				
Bacillus thuringiensis var. israelensis Bactimos; BMC; Skeetal; Teknar; Vectobac *Bacillus turingiensis*, variety *israelensis*		larvacide for mosquitoes and some other flies				water: "insoluble"

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long Term Toxicity (Chronic)	
Bacillus thuringiensis var. kurstaki Agritol; Attack; Bactospeine; Bactur; Bakthane; Biotrol; BTV; Bug Time; Cekubacillina; Dipel; Foray; Javelin; Larvatrol; Leptox; Novabac; Thuricide; Tribactur *Bacillus thuringiensis*, variety *kurstaki*		larvacide for moths				water: [illegible]
Bacillus thuringiensis var. san diego M-One *Bacillus thuringiensis*, variety *san diego*		larvacide for some beetles				
Bacillus thuringiensis var. tenebrionis Trident *Bacillus thuringiensis*, variety *tenebrionis*		larvacide for some beetles				
bromadiolone Apobas; bromakil; Bromatrol; Bromone; Bromorat; Canadien 2000; Deadline; Deturi Ratones; Lanirat; Maki; Musal; Ratinus; Rodine-C; Slaymore; Spyant Ratones; Super Asecho; Super-Caid; Super-Rozol; Temus; Topidion 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxy-2*H*-1-benzopyran-2-one; 3-[-[*p*-(*p*-bromophenyl)-hydroxyphenethyl]-benzyl-4-hydroxycoumarin] CAS # 28772-56-7	coumarin	rodenticide	?	oral: very high (1) dermal: ? inhalation: ?	?	immediate toxicity: fish: high (2) water: "insoluble" "nonflammable"
butachlor Butanex; Butanox; CP 53619; Lambast; Machete; Rasayanchlor *N*-(butoxymethyl)-2-chloro-2',6-diethylacetanilide; *N*-(butoxymethyl)-2-chloro-*N*-(2,6-diethylphenyl) acetamide CAS # 23184-66-9	amide	herbicide not registered: USA	non-pers (1)	oral: medium (1,2) dermal: medium (2) inhalation: medium (1)	suspect mutagen (3)	immediate toxicity: fish: medium to high (1) birds: low to medium (1) water: slightly soluble slightly volatile combustible
captafol Bayleton Triple (with triadimefon & carbendazim); Crisfolatan; Difolatan; Difosan; Folcid; Foltapet (with folpet); Haipen; Merpafol; Mycodifol; Ortho 5865; Sanspor; Sufonimide; Sulfemmide *cis*-*N*-[(1,1,2,2-tetrachloroethyl)thio]-4-cyclohexene-1,2-dicarboximide CAS # 2425-06-1	phthalate	fungicide cancelled USA, 1986	non-pers (1)	oral: low (2) dermal: medium (3) inhalation: ?	carcinogen (4,5) suspect mutagen (6,7) suspect teratogen (6,8)	immediate toxicity: fish: very high (10) birds: low (9) aquatic insects: very high (10) crustaceans: very high (10) water: slightly soluble

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
transformation product(s): **delta[4] tetrahydrophthalimide** CAS # 85-40-5					suspect fetotoxin (1)	
carbanolate Banol; Sok; U-12927 6-chloro-3,4-xylyl methylcarbamate; 2-chloro-4,5-dimethylphenyl methylcarbamate CAS # 671-04-5	carbamate	insecticide	?	oral: very high (1) dermal: ? inhalation: ?	?	immediate toxicity: bees: high (2)
carbaryl Arylam; Bercema NMC50; Carpolin; Crag Sevin; Dicarbam; Dyna-carbyl; Germain's; Hexavin; Karbatox 75; Menaphtham; Nac; Pomex; Ravyon; Sevin; Sok; Tercyl; Tricarnam; UC 7744; Vioxan; Zrylam 1-naphthyl methylcarbamate; methylcarbamate 1-naphthalenol CAS # 63-25-2	carbamate	insecticide acaricide mollusicide	non-per to mod-pers (1,2)	oral: medium to high (3) dermal: ? inhalation: low	suspect carcinogen (5) suspect mutagen (6) teratogen (4) fetotoxin (6) suspect viral enhancer (6) decreased fertility from ovary and testes damage through successive generations (7)	immediate toxicity: birds: low to medium (3) fish: very high (10) bees: "extremely toxic" (6) crustaceans: very high (6) earthworms: "extremely toxic" (10) aquatic worms: high to very high (11) aquatic insects: very high (10) plants: toxic to some; chromosome damage in some (12) long-term toxicity: birds: may affect breeding success (8,9) fish: reduction in sex hormone, may affect reproduction (13); increased vulnerability to predation; affects swimming capacity (14) water: slightly soluble to soluble slightly volatile combustible
transformation product(s): **1-naphthol** *α*-naphthol CAS # 90-15-3	miscel-laneous			oral: high (1)	liver damage (1)	
nitrosocarbaryl from reaction with nitric acid often present in air, soil, saliva when carbaryl is ingested					carcinogen (1) mutagen (1,2)	
carbendazim BCM; BMC; Carbate; carbendazol; Cekudazim; CTR 6669; Custos; Delsene; Delsene M; Equitdazin; Focal; Hoe 17411; Kemdazin; Lignasan; MBC*; MCB; Pillarstin; Supercarb; Tritocol 2-(methoxycarbonylamino)-benzimidazole; methyl 1*H*-benzimidazol-2-yl-carbamate; methyl-2-benzimidazole carbamate *MBC also used as a trade name for sodium chlorate CAS # 10605-21-7	benzimi-dazole	fungicide	mod-pers	oral: low to medium dermal: low to medium inhalation: ?	suspect carcinogen suspect mutagen testes damage	immediate toxicity: birds: low fish: low to high earthworms: "very toxic' water: slightly soluble non-volatile

Source: Rachel Carson Council Inc. USA

NAME Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
carbofuran Barbodan; BAY 78537; Brifur; Bripoxur; Carma (with isofenphos); Chinufur; Curaterr; D 1221; FM 10242; Furacarb; Furadan; Furadan 15G; Kenofuran; NIA 10242; Yaltox 2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate CAS # 1563-66-2	carbamate	insecticide nematocide acaricide	non-pers to mod-pers (1,2)	oral: high to very high (2,3) dermal: ? inhalation: ? "carbofuran is high toxic by the oral, dermal, and inhalation routes of exposure" (4)	suspect mutagen (3) immunotoxin (5)	immediate toxicity: birds: very high (3,6) fish: high to very high (2) water: soluble slightly volatile
carbon disulfide carbon bisulfide CAS # 75-15-0	metal\mineral sulfur	fumigant insecticide herbicide fungicide rodenticide soil sterilant nematocide	?	oral: ? dermal: ? inhalation: "highly poisonous" (1)	neurotoxin (2) heart damage (3) fetotoxin (3) liver damage (3) kidney damage (3) thyroid, adrenal changes (3)	water: soluble highly volatile flammable
carbon tetrachloride Granosan (with ethylene dichloride); Necatorina perchloromethane; tetrachloromethane CAS # 56-23-5 "susceptibility to carbon tetrachloride poisoning is enhanced by the contemporaneous use of alcohol" (8)	organo-chlorine	insecticide fumigant cancelled USA, 1986	?	oral: low to medium (1,2) dermal: ? inhalation: low (1)	carcinogen (2,3) fetotoxin (2) liver damage (4,5) eye damage (6) kidney damage (6) testes damage (7)	water: "very slightly soluble" "non-inflammable"
transformation product(s): **phosgene gas**				inhalation: "danger period is usually 6 to 24 hours after exposure" (1)	lung damage (2)	water: "slightly soluble" highly volatile "nonflammable gas"
carbophenothion Acarithion; Dagadip; Endyl; Garrathion; Hexathion; Lethox; Nephocarp; R-1303; Stauffer; Trithion *S*-[(*p*-chlorophenylthio)methyl *O,O*-diethyl phosphorodithioate; *O,O*-diethyl *S*-[(*p*-chlorophenylthio)-methyl]phosphorodithioate CAS # 786-19-6	organo-phosphate	insecticide acaricide	?	oral: very high (1) dermal: high to very high (2) inhalation: ?	?	immediate toxicity: birds: high to very high (3) fish: high to very high (4) crustaceans: very high (4) amphibians: very high (5) bees: high (6) water: slightly soluble volatile
carboxin Arrest 75W; Ceravax; D 735; DCMO; Kemekar; Pro-Gro; Quinolate V4 X AC, FS, DS (with oxine-copper & anthraquinone; Uniroyal D 735; Vitaflo; Vitavax; Vitavax 100 5,6-dihydro-2-methyl-*N*-phenyl-1,4-oxathiin-3-carboxamide; 2,3-dihydro-5-carboxanilido-6-methyl-1,4-oxathiin; 5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxanilide CAS # 5234-68-4	amide	fungicide	non-pers (1,2)	oral: medium to high (3,4) dermal: low to medium (3) inhalation: low (1)	?	immediate toxicity: birds: low to medium (1,5) fish: high (5) crustaceans: low (5) bees: low (6) aquatic insects: low (5) water: soluble combustible

Source: Rachel Carson Council Inc. USA

Factsheets on Pesticides

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
chlorobenzilate Acaraben; Akar; Benz-O-Chlor; Benzilan; Compound 338; Folbex; G 23992; Geigy 338; Kop-Mite ethyl 4,4'-dichlorobenzilate CAS # 510-15-6	organo-chlorine	acaricide restricted USA, 1979	non-pers (1)	oral: medium (2) dermal: ? inhalation: low (1)	carcinogen (3,4) testes damage (1,4)	immediate toxicity: birds: low (1) fish: high (1) bees: low (5) water: slightly soluble slightly volatile
chlorofluorocarbons Freon Genetron 1,2-dichloro-1,1,2,2-tetrafluorethane CAS # 76-12-0	miscel-laneous	aerosol propellant almost all pesticide uses banned, USA	?	oral: ? dermal: ? inhalation: low (1)	see piperonyl butoxide (1)	long-term toxicity: reduction in protective ozone layer in earth's stratosphere, producing a global increase in ultraviolet radiation at the earth's surface; increase in skin cancers and mutation rates; may also cause climate changes
transformation product(s): **chlorine** (see chlorine)						
phosgene gas (see carbon tetrachloride)						
chlorothalonil Blazon; Bravo; Bravo C/M; Bravocarb (with carbendazim); chlorthalonil; Clortocar Ramato; Clortosip (with copper oxychloride & maneb); Dacobre; Daconil 2787; Exotherm; Exotherm Termil; Forturf; Nopocide; Termil tetrachloroisophthalonitrile CAS # 1897-45-6	benzo-nitrile	fungicide	mod-pers (1,2)	oral: low (3) dermal: low to medium (3) inhalation: high (3)	carcinogen (4,5) hyperexcitability (5) skin damage (6) eye damage (7) kidney damage (5)	immediate toxicity: birds: low to medium (1) fish: very high (1) bees: low (9) "aquatic organisms": very high (1) plants: toxic to some (10) water: insoluble oil: slightly soluble slightly volatile
transformation product(s): **4-hydroxy-2,5,6-trichloroisophtalonitrile**					anemia (1)	immediate toxicity: birds: medium (1)

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NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
chlorpyrifos Dowco 179; Dursban; Lepister (with flucythrinate); Lorsban; Pyrinex; Salut (with dimethoate) O,O-diethyl O-3,5,6-trichloro-2-pyridyl phosphorothioate CAS # 2921-88-2	organo-phosphate	insecticide	mod-pers (1)	oral: medium to high (1,2) dermal: medium to high (3,4) inhalation: high (6)	cumulative (13,14) fetotoxin (6) delayed neurotoxin (7) bulls: sterility and impotence (8)	BIOCIDE immediate toxicity: birds: high to very high (1,9) molluscs: very high (1) fish: very high (1) amphibians: low to high (2) crustaceans: very high (1) bees: very high (10) aquatic insects: very high (1) long-term toxicity: birds: leg weakness (1); delayed neurotoxicity (11) fish: affects growth (1) crustaceans: affects reproduction & equilibrium (1) plants: toxic to some (12) water: slightly soluble slightly volatile
contaminant(s): **sulfoTEPP** (see sulfoTEPP)						
transformation product(s): **pyridinol** 3,5,6-trichloro-2-pyridinol						slightly volatile
cinmethylin Argold; Cinch exo-1-methyl-4-(1-methylethyl)-2-[(2-methylphenyl)methoxy]-7-oxabicyclo[2.2.1]heptane CAS # 87818-31-3	miscel-laneous	herbicide	mod-pers (1)	oral: medium (2) dermal: low to medium (1) inhalation: ?	?	water: slightly soluble slightly volatile combustible
copper hydroxide Blue Shield; Champion; Comac Parasol; Criscobre; Cudrox; Cuidrox; Cupravit Blue; Kocide; Kocide 101; Kocide 404S; Parasol copper (II) hydroxide; cupric hydroxide; hydrated cupric oxide CAS # 20427-59-2	inorganic	antibiotic fungicide		oral: medium (1)	"causes irreversible eye damage" (2)	immediate toxicity: birds: low to medium (1) fish: low to high (1) water: slightly soluble
copper oxide Caocobre; Copox; Copper-Sandoz; Copper-Sardez; Cuprocide; Fungi-Rhap; Kuprite; Nordox; Oleocuivre; Perecot; Perenox; Triangle*; Yellow Cuprocide brown copper oxide; cuprous oxide; dicopper oxide *see Bordeaux mixture CAS # 1317-39-1	inorganic	fungicide developed to replace Bordeaux mixture		oral: medium to high (1,2)		immediate toxicity: fish: low (2) bees: "harmless to bees" (3) water: "insoluble"

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
copper sulfate Blue Copperas; Blue Vitriol; Bluestone; Copace-E; Copperfine-Zinc; Foltimil (with folpet); Neutrocrop; Nu-Cop; Phyton 27; Spray-Cop; Triangle* basic copper sulfate; copper sulfate monohydrate; copper sulfate pentahydrate *See Bordeaux mixture CAS # 7758-98-7	inorganic	fungicide herbicide algacide		oral: medium to high (1,2) dermal: low to medium (2) inhalation: low to high (2)	mutagen (4,5) "bioaccumulates" (3)	immediate toxicity: fish: low to very high (1,2) bees: "toxic" crustaceans: low (2) molluscs: medium (2)
copper sulfate monohydrate	inorganic	fungicide				immediate toxicity: fish: "toxic to fish" (1)
copper tea complex Algae-Rhap CU; K-Pool; K-Tea copper triethanolamine complex	organic	algacide herbicide				immediate toxicity: fish: medium (1) water: soluble
copper zinc chromate Crag Fungicide 658; Experimental Fungicide 658	inorganic	fungicide antibiotic				water: "practically insoluble"
cupric hydrazinium sulfate Mathieson 466; Omazene; Omazine copper (II) dihydrazinium disulfate; bis(hydrazine)bis(hydrogensulf ato)copper; copper dihydrazine disulfate CAS # 33271-65-7	organic	fungicide				
oxine-copper Bioquin; Copper 8; Copper Oxinate; Cunilate 2472; Cuproquin; Dokirin; Dormycin; Fruitdo; Milmer 1; Quinolate; Quinolate 15; Quinolate 20; Quinolate AC, Fs, Quinolate AC Kara (with anthraquinone); Quinolate MG SAFI (with endosulfan & lindane); Quinolate Triple Kara (with anthraquinon & lindane); Quinolate V 4 X AC, FS, DS (with anthraquinone & carboxin); Quinolate V 4 X Triple (with lindane); Tomo-oxiran CAS # 10380-28-6	organic	fungicide wood preservative		oral: low to medium (1)	suspect mutagen (2)	immediate toxicity: fish: high (3) water: "insoluble" "non-volatile"
cyfluthrin Baygon Spray (with dichlorvos & propoxur); Baythroid F (with omethoate); Baythroid TM (with acephate-met); Insectipen; Muscatox (with phoxim) *(RS)-α*-cyano-4-fluo ro-3-[phenoxybenzyl (1*RS*)-*cis,trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate CAS # 68359-37-5	pyrethroid	insecticide	non-pers to mod-pers (1)	oral: low to very high (2,3) dermal: ? inhalation: ?	?	immediate toxicity: fish: high to very high (1,4) crustacean: very high (5) bees: high (6) water: insoluble to slightly soluble non-volatile to volatile flammable

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Factsheets on Pesticides

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
cymoxanil Bayleton AN, Curzatem (with triadimefon); Fytospore (with mancozeb) 1-(2-cyano-2-methoxymino-acetyl)-3-ethylurea	urea	fungicide not registered for use in U.S.	non-pers (1)	oral: medium (1) dermal: ? inhalation: ?	?	immediate toxicity: fish: medium (1) water: soluble
cypermethrin Ammo; Arrivo; Barricade; Cymbush; Cymperator; Cypercopal; cypermethrine; Cyrux; Demon; Fenom; Flectron; Folcord; Imperator; Kafil Super; Nurelle; Polytrin; Ripcord; Siperin; Toppel; Ustaad; WL 43467 (*RS*)-α-cyano-3-phenoxybenzyl (1*RS-cis,trans*-3-9 2,2-dichlorovinyl)-2,2-dimethyl-cyclopropanecarboxylate CAS # 52315-07-8	pyrethroid	insecticide	non-pers (1)	oral: medium to high (2,3) dermal: ? inhalation: ?	mutagen (4,5) immunotoxin (6)	immediate toxicity: birds: low (7,8) fish: high to very high (1,9) crustaceans: very high (10) bees: "toxic" (2) water: insoluble oil: "lipophilic" non-volatile
2,4-D Agricorn D; Agrotect; Amidox; Cloroxone; College Brand Weed Killer; Ded-Weed Aero Ester; Demise; Dicotox; Dinoxol; Dymec; Esteron 44; Fersone; Green Cross Amine 80; Hormotox; Lawn-Keep; Lithane; Miracle; Niagara Am Sol; Plantgard; Raid Weed Killer; Weedone 2,4-dichlorophenoxyacetic acid CAS # 94-75-7	phenoxy	herbicide restricted USA	non-pers to mod-pers (1,2)	oral: medium to high (2,3) dermal: high (4) inhalation: medium to high (5)	carcinogen (6,7) suspect mutagen (8,9) teratogen (10,11) suspect fetotoxin (12) anorexia (12) immunotoxin (13) toxic injury to liver, kidney, & central nervous system (19)	immediate toxicity: birds: low to high (5,14) fish: low to very high (5,15) amphibians: low to medium (5) crustaceans: low to very high (5) molluscs: medium (11) non-target insect: low to high (11) bees: low to medium (16) soil organisms: low (17) long-term toxicity: birds: can affect egg production (17) fish: cumulative (17) amphibians: inhibits frog egg development (17) crustaceans: may significantly reduce population (17) molluscs: reduction in population; cumulative (17) plants: leaf malformation (16) soil organisms: may inhibit growth (17) can favor growth of insects and pathogens (18)

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
2,4-D (*cont.*)						water: "insoluble" to soluble" oil: "insoluble" highly volatile
transformation product(s): **2,7-dichlorodibenzo-p-dioxin**	dibenzo-dioxin				carcinogen (1)	slightly volatile
1,3,7-trichlorodibenzo-p-dioxin (see dibenzodioxin class)	dibenzo-dioxin					
1,3,6,8-tetrachlorodibenzo-p-dioxin 1,3,6,8-TCDD	dibenzo-dioxin					water: insoluble
1,3,7,9-tetrachlorodibenzo-dioxin	dibenzo-dioxin					
TCDD (see chloroneb)						
2,4-dichlorophenol						
dazomet Basamid; Crag Fungicide 974; Crag Nemacide; DMTT; Micro-Fume; Mylone; N-521; Preservit	miscel-laneous	herbicide fungicide nematocide	non-pers to mod-pers (1,2)	oral: medium to high (3) dermal: ?	liver and kidney damage (6)	immediate toxicity: fish: "toxic to fish" (4) bee: low to medium (5)

(*continued on next page*)

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
dazomet (*cont.*) tetrahydro-3,5-dimethyl-2H-l,3, 5-thiadiazine-2-thione; 3,5-dimethyl-2H-l,3,5-thiadiazine-2-thione CAS # 533-74-4				inhalation: medium (3)		water: soluble volatile "nonflammable"
transformation product(s): **carbon disulfide** (see carbon disulfide)						
methyl isothiocyanate (see methyl isothiocyanate)						
formaldehyde (see formaldehyde)						
hydrogen sulfide (see calcium polysulfide)						
2,4-DB Butoxone (with 2,4-D & MCPA); Butoxone SB; Butyrac 118; Butyrac ester; Embutox; Ley-Cornox (with benazolin & MCPA); MB 2878 4-(2,4-dichlorophenoxy) butyric acid CAS # 94-82-6	phenoxy	herbicide	non-pers (1)	oral: medium (1) dermal: low to medium (2)	mutagen (2)	immediate toxicity: fish: medium (2) bees: low to medium (3) water: slightly soluble oil: "highly soluble"
salt(s): **2,4-DB sodium** CAS # 10433-59-7				oral: medium to high (1)		
transformation product(s): **2,4-D** (see 2,4-D)						

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Factsheets on Pesticides

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
DDT Anofex; Arkotine; Chlorophenothane; Dedelo; Diamekta 50%; Didimac; Dinocide; Genitox; Gesapon; Gesarex; Gyron; Ixodex; Kopsol; Neocidol; Pentachlorin; Pentech; Rukseam; Santobane; Tech DDT; Zerdane dichloro diphenyl trichloroethane; 1,1,1,-trichloro-2,2,-bis(p-chlorophenyl) ethane CAS # 50-29-3	organo-chlorine	insecticide cancelled USA, 1972	pers (1)	oral: high (2) dermal: medium to high (3) inhalation: ?	cumulative (3) carcinogen (4) mutagen (5) fetotoxin (5) embryotoxin (3) decreased fertility (3) hormone changes (6) aplastic anemia (6) liver damage (7) immunotoxin (8)	BIOCIDE immediate toxicity: birds: low to medium (9) fish: very high (10) amphibians: low to medium (9) crustaceans: very high (10) bees: high (11) aquatic insect: very high (10) aquatic worm: low (12) long-term toxicity: birds: diminished reproduction; eggshell thinning; cumulative (9,13) fish: affects reproduction (1) snakes: much more toxic to egg-laying than to viviparous snakes (14) reduced photosynthesis by marine phytoplankton (15) bioaccumulates (16) molluscs: reduces shell growth (17) water: insoluble oil: "very soluble" slightly volatile
transformation product(s): **dicofol** (see dicofol)						
DDE (see DDE)						
DDD (see DDD)						
deltamethrin Butoss; Cislin; Crackdown; decamethrin; Decis; Decis Dan (with endosulfan & fenitrothion & profenfos); Delsekte; deltamethrine; Deltaphos (with triazophos); Detrans (with esbiothrin); K-O (with esbiothrin & piperonyl butoxide); K-Obiol (with piperonyl butoxide); K-Otek; K-Othrin; Kothrin; NRDC 161; OMS 1998; RU 22974 [1*R*-[1α(S*),3α]]-cyano(3-phenoxyphenyl) methyl 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate CAS # 52918-63-5	pyrethroid	insecticide	?	oral: medium to very high (1,2) dermal: ? inhalation: ?	?	water: insoluble non-volatile

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
diazinon AG 500; Alfa-tox; Basudin; Dazzel; Diazajet; Diazatol; Diazide; Diazinon; Diazitol; Diazol; dimpylate; Dipofene; G 24480; Gardentox; Knox Out 2FM; Neocidol; Nipsan; Sarolex; Spectracide O,O-diethyl O-(2-isopropyl-6-methyl-4-pyrimidinyl) phosphorothioate CAS # 333-41-5	organo-phosphate	insecticide nematocide banned from use on golf courses and turf farms in USA	non-pers (1,2)	oral: medium to high (3,4) dermal: low to high (4) inhalation: medium (3)	suspect mutagen (5,6) fetotoxin (7) suspect neurotoxin (8) allergic dermatitis (9) conjunctivitis (9) immunotoxin (10)	BIOCIDE immediate toxicity: birds: very high (1,11) fish: very high (12) amphibians: very high (11) crustaceans: very high (12) bees: very high (13) aquatic insects: very high (14) aquatic worm: high (9) plants: toxic to some (15) long-term toxicity: birds: teratogen (2) water: slightly soluble oil: very soluble volatile combustible
contaminant(s): **isodiazinon**					porphyria (1)	
transformation product(s): **sulfoTEPP** (see sulfoTEPP)						
TEPP (see TEPP)						
dichloropropene D-D (with 1,2-dichloropropane); D-D92; DCP; Dedisol C; Dorlone II; Nematox (with 1,2-dichloropropane); Nematox II; Telone (with 1,2-dichloropropane); Telone II 1,3-dichloropropene; 1,3-dichloro-1-propene CAS # 542-75-6	organo-chlorine	soil fumigant nematocide	"non-pers" (1)	oral: high (2) dermal: high (2) inhalation: ?	carcinogen (3,4) suspect mutagen (1,5) liver & kidney damage (1,5)	immediate toxicity: fish: medium to high (6,7) crustaceans: very high (7) bees: low to medium (8) water: soluble highly volatile flammable

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NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
dichlorvos Apavap; Atgard; Aygard V; Benfos; Brevinyl; Brevinyl E50; Canogard; DDVP; Dedevap; Devikol; Divipan; Equigel; Mafu Strip; No-Pest Insecticide Strip; Raid Ant & Roach Killer; Raid Solid Insect Killer; SD 1750; Task; Unifos; Vaponite (in no-pest strips & some flea collars) *O,O*-dimethyl-2,2-dichlorovinyl phosphate; 2,2-dichlorovinyl dimethyl phosphate CAS # 62-73-7	organo-phosphate	insecticide	non-pers (1,2)	oral: high (3) dermal: high to very high (4) inhalation: high (3,5)	carcinogen (2,6) mutagen (3,7) suspect teratogen (2,3) sperm and other reproductive abnormalities (3) kills human white blood cells (8) inhibits steroid synthesis (9) indications of bone marrow damage and aplastic anemia (10) immunotoxin (11)	immediate toxicity: birds: very high (12) fish: very high (13) bees: very high (1) crustaceans: very high (13) aquatic insects: very high (13) long-term toxicity: birds: delayed neurotoxin (11) water: soluble oil: very soluble highly volatile combustible
diclofop-methyl dichlofop-methyl; dichlorfop-methyl; diclofop; Hoegrass; Hoelon; Illoxan; One Shot (with bromoxynil & MCPA) 2-(4-(2,4-dichlorophenoxy)phenoxy)-propanoic acid methyl ester; methyl 2-(4-(2,4-dichlorophenoxy)phenoxy)-propionate CAS # 51338-27-3	phenoxy	herbicide	non-pers to mod-pers (1,2)	oral: medium (2,3) dermal: medium to very high (2) inhalation: ?	?	immediate toxicity: birds: low to medium (2) fish: medium to high (2) water: slightly soluble to very soluble slightly volatile to highly volatile flammable
dicofol Acarin; Acavers 35 (with methomyl); FW-293; Kelthane; Kethane Mixte (with methyl parathion); Mitigan; Mixte (with methyl parathion); Parasoufre Acaricide (with methyl parathion & sulfur); Tedane Extra (with dinocap & tetradiforn or mancozeb); Tuver Acaricide (with ethion & methyl parathion) 1,1-bis(*p*-chlorophenyl)-2,2,2-trichloroethanol; 4,4'-dichloro-*α*-(trichloromethyl)benzhydrol CAS # 115-32-2	organo-chlorine	insecticide acaricide	mod-pers (1)	oral: medium to high (2,3) dermal: medium to very high (2,3) inhalation: ?	carcinogen (4)	immediate toxicity: birds: medium to high (5) fish: very high (6) crustaceans: low (7) bees: low (8) aquatic insects: very high (6) water: "insoluble" oil: "soluble" flammable

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
contaminant(s):						
DDT (see DDT)						
DDE (see DDE)						
DDD (see DDD)						
dieldrin Alvit; Anter; Compound 497; dieldrine (France); Dielmoth; Dorytox; Dudubitoke; Eldrinol; HEOD (Canada); Hododrex; Illoxol; Kyadrin; Octalox; Pestex; Red Shield hexachloroepoxyoctahydro-*endo*-*exo*-dimethanonaphthalene and related compounds; 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro 1,4-*endo*-*exo*-5, 8-dimethanonaphthalene and related compounds CAS # 60-57-1	organo-chlorine	insecticide cancelled USA, 1971	pers (1)	oral: high to very high (2) dermal: very high (2) inhalation: very high (19)	cumulative (3,4) suspect carcinogen (1,5,6) suspect teratogen (7,8) immunotoxin (9,10) abnormal brain waves, behavior changes (10,11)	BIOCIDE immediate toxicity: birds: high to very high (12) fish: very high (13) amphibians: very high (1) crustaceans: very high (14) molluscs: very high (1) bees: very high (15) aquatic insects: very high (13) aquatic worms: medium (16) plankton: very high (14) long-term toxicity: birds: damages reproduction, eggshell thinning (17,18) water: insoluble oil: very soluble slightly volatile "nonflammable"
transformation product(s):						
photodieldrin 2a,2,2,4,5,5a-hexachlorodecahydro-2,4,6-metheno-2H-cychlopenta [4,5]pentaleno[1,2-]oxirene CAS # 13366-73-9				"more toxic than dieldrin" (1)		
diflubenzuron deflubenzon; diflubenuron; difluron; Dimilin; Dimilin IG; Dimilin W-25; Micromite; OMS 1804; PH 60-40; TH 60-40; Vigilante *N*-[[(4-chlorophenyl)amino] carbonyl]-2,6-difluorobenzamide CAS # 35367-38-5	urea	insecticide restricted use in USA	non-pers to mod pers (1-3)	oral: low (4) dermal: low (4) inhalation: low (4)	affects oxygen carrying capacity of red blood cells via methemoglobinemia and sulfemoglobinemia (3,5)	immediate toxicity: birds: low (4) fish: low (4) crustaceans: very high (4) long-term toxicity: crustaceans: affects reproduction (6) water: "soluble" oil: "virtually insoluble"
transformation product(s):						
4-chloroaniline CAS # 10-64-7					carcinogen (1) may cause methemoglobinemia and sulfhemoglobinemia (2)	

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
dimethoate Bio Long Last (with permethrin); Bio Systemic Insecticide; Cyanotril (with flucythrinate); Cygon; Cykuthoate; Daphene; Devigon; Dimet; Dimethogen; Flutrin (with flucythrinate); fosfamid (USSR); Fostion MM; Mikantop (with fenvalerate); Perfekthion; Rogor; Roxion; Salut (with chlorpyrifos); Trimetion; Turbair Systemic Insecticide; Vitex *O,O*-dimethyl *S*-(*N*-methylcarbamoylmethyl) phosphorodithioate; 2-dimethoxyphosphinothioylthio-*N*-methylacetamide CAS # 60-15-5	organo-phosphate	insecticide acaricide cancelled, most products, USA, 1981	non-pers (1,2)	oral: high to very high (2,3) dermal: high to very high (1,2) inhalation: ?	suspect carcinogen (4) mutagen (2,5) suspect teratogen (2,6) blood damage (7) testicular atrophy (4) kidney damage (4) immunotoxin (8)	immediate toxicity: - birds: high to very high (1,2) fish: low to high (1,2) crustaceans: high to very high (2,9) bees: very high (10) aquatic insects: very high (2) water: very soluble slightly volatile flammable to combustible
transformation product(s): **omethoate** (see omethoate)						
dinocap Acarthane (with dicofol); Arathane; Cakucap; Crotothane; Iscothane; Karathane; Mildane; Mildex; Sialite; Tedane Extra (with dicofol & tetradiforn or w/ mancozeb) 2-(1-methylheptyl)-4,6-dinitrophenocrotonate CAS # 39300-45-3	phenol	fungicide acaricide restricted USA, 1989	non-pers to mod-pers (1,2)	oral: medium (1) dermal: ? inhalation: high (1)	teratogen (3,4)	immediate toxicity: fish: very high (5) bees: medium (6) water: insoluble highly volatile
diuron Cekiuron; Dailon; DCMU; Destral (with dalapon & 2,4-D); Di-on; Diurex; DMU; Dynex; Gramixel (with paraquat); Gramuron (with paraquat); Karmex; Krater (with asulam); Marmer; Paracol (with paraquat); Rassapron (with atrazine & amitrole); Surefire (with paraquat); Totacol (with paraquat); Weed-Free g (with bromacil) 3-(3,4-dichlorophenyl)-1,1-dimethylurea CAS # 330-54-1	urea	herbicide	mod-pers to pers (1,2)	oral: medium (3) dermal: low to medium (4) inhalation: ? poisoning potential increased with protein-deficient diet (5)	suspect mutagen (6) suspect teratogen (7) growth inhibition (5) anemia (5)	BIOCIDE immediate toxicity: birds: low to medium (8) fish: medium to high (9) crustaceans: medium to high (9) bees: low (10) aquatic insects: high (9) phytoplankton: "very high" (2) long-term toxicity: fish: gill damage, inhibits reproduction (2) molluscs: shell growth inhibited (2) can reduce oxygen content of ponds (2) water: slightly soluble oil: soluble non-volatile "nonflammable"
contaminant(s): **TCAB** TCAB 3,4,3',4'-tetrachloroazobenzene structure is analogous to TCDD (see under 2,4,5-T) CAS # 14047-09-7		also a component of diuron			suspect mutagen (1,2) chloracne & hyperkeratosis (3)	

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
dodine AC 5223; Carpene; Curitan; Cyprex; Cyprex 65W; dodin; dodine acetate; doguadine (France); Efuzin; Melprex; Mexprex; Syllit; Triododine; tsitrex (USSR); Venturol; Vondodine dodecylguanidine acetate; laurylguanidine acetate CAS # 2439-10-3	miscellaneous	fungicide herbicide	?	oral: medium (1) dermal: low to high (1) inhalation: high (2)	?	immediate toxicity: birds: medium (3) fish: high (3) bees: low to medium (4) insect predators: "toxic to some" (5) water: soluble volatile
edifenphos BAY 78418; ediphenphos; Hinosan; SRA 7847 *O*-ethyl-*S*,*S*-diphenyl phosphorodithioate CAS # 17109-49-8	organophosphate	fungicide	non-pers (1)	oral: high (2) dermal: ? inhalation: high (2)	?	immediate toxicity: birds: medium (2) fish: high (2) water: "practically insoluble" volatile
endosulfan benzoepin; Beosit; Chlorthiepin; Cyclodan; Endocel; FMC 5462; Hoe 2671; Insectophene; Kop-Thiodan; Malic; Malix; NIZ 5462; Quinolate MG SAFI (with oxine-copper & lindane); Rogodan (with dimethoate); Thifor; Thimul; thiodan (Iran, USSR); Thionex; Tiovel hexachlorohexhydromethano-2,4,3-benzodioxathiepin oxide; 6,7,8,9,10,10-hexachloro-1,5,5*a*,6,9,9*a*-hexahydro-6,9-methano-2,4,3-benzodioxathiepin 3-oxide; 5-norbornene-2,3-dimethanol-1,4,5,6,7,7-hexachlorocyclic sulfite CAS # 115-29-7	organochlorine	insecticide	mod-pers (1)	oral: very high (2) dermal: very high (2) inhalation: very high (2)	suspect carcinogen (4) mutagen (5,6) kidney damage (4) eye damage (7) suppression of immune responses (8) red blood cell damage (9)	BIOCIDE immediate toxicity: birds: high to very high (10) fish: very high (11) crustaceans: very high (11) bees: very high (12) amphibians: very high (13) molluscs: very high (14) long-term toxicity: fish: ovary damage (15,16) crustaceans: cumulative (18) can inhibit fungal growth (17) damages some plants: some flowers, grapes, and birches (19) water: insoluble slightly volatile "nonflammable"
ethephon Arvest; Bromaflor; Cagro; Cepha; Cerone; Composan; Etheverse; Ethrel; Flordimex; Florel; Prep; Terpal C (with chlormequat chloride); Terpal M (with chlormequat chloride & mepiquat chloride) 2-(chloroethyl)phosphonic acid CAS # 16672-87-0	organophosphate	plant growth regulator	non-pers (1)	oral: medium (1,2) dermal: medium (2) inhalation: ?	?	immediate toxicity: birds: medium (1) fish: low (2) bees: low to medium (3) crustaceans: low (4) water: soluble oil: "insoluble" "nonflammable"

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
ethion Acarfor (with dicofol); diethion (France, India, So. Africa); Embathion; Ethanox; Ethiol; Ethodon; FMC 1240; Hylemox; Itopaz; Kwit; NIA 1240; Niagara 1240; Nialate; Rhodiacide; Rhodocide; RP-Thion; Tuver Acaricide (with dicofol & methyl parathion); Vegfru Fosmite *O,O,O',O*-tetraethyl *S,S'*-methylene bisphosphorodithioate; *S',S'*-methylene *O,O,O',O*-tetraethyl di(phosphorodithioate); *S',S'*-methylene bis(*O,O*-diethyl phosphorodithioate) CAS # 563-12-2	organo-phosphate	insecticide acaricide	non-pers to mod-pers (1)	oral: high to very high (3,4) dermal: high to very high (1,4) inhalation: medium to high (4,5)	?	immediate toxicity: birds: low to medium (6) fish: medium to high (7) crustaceans: medium to high (7) bees: medium (8) aquatic insects: medium (7) long-term toxicity: birds: teratogen (9) water: slightly soluble oil: "soluble" slightly volatile "nonflammable"
ethylene dibromide Aadibroom; Agrogas; Bromofume; Carboxide; Cartox; Celmide; DM23 Forte; Dowfume EDB; E-D-Bee; EDB; Edesol; Fumo-Gas; Granosan; Iscobrome D; Nemtosol; Nephis; Soilbrom 40; Soilbrom-90EC; Tradiafume; Unifume 1,2-dibromoethane CAS # 106-93-4 CAS # 22224-92-6	miscel-laneous	fumigant insecticide cancelled, USA, 1989	non-pers to pers (1,2)	oral: high (3) dermal: high (4) inhalation: ?	carcinogen (5) mutagen (2,6) suspect teratogen (7,8) liver, kidney, heart, & spleen damage (9) sperm & egg damage (5) disulfiram enhances toxic effects of EDB (5)	immediate toxicity: birds: high (10) fish: medium (11) long-term toxicity: fish: liver & kidney damage (12) plants: mutagen (13) bioaccumulates (3) water: soluble highly volatile "nonflammable"
fenarimol Bloc; EL-222; Fenzol; Rimidin; Rimidine Plus (with carbendazim & maneb); Rubigan; Transflo 2,4'-dichloro-*α*-(pyrimidin-5-yl) benzhydryl alcohol; 3-(2-chlorophenyl)-3-(4-chloro-phenyl)-5-pyrimidinemethanol CAS # 60168-88-9	miscel-laneous	fungicide	mod-pers (1)	oral: medium (2) dermal: ? inhalation: ?	suspect carcinogen (3) teratogen (4) decreased male fertility (5)	immediate toxicity: fish: high (1) water: slightly soluble slightly volatile
fenitrothion Accothion; Agrothion; BAY 41831; Cyfen; Cytel; Danathion; Debucol; Dicontal Neu (with trichlorfon); Docofen; Fenitox; Fenstan; Folithion; MEP; Novathion; Nuvanol; Pesguard ANS (with tetramethrin); S 5660; Sumimix (with fenpropathrin); Verthion *O,O*-dimethyl O-(4-nitro-*m*-tolyl) phosphorothioate CAS # 122-14-5	organo-phosphate	insecticide acaricide	non-pers (1)	oral: medium to high (2) dermal: high (2) inhalation: ?	suspect mutagen (3) suspect viral enhancer, implicated in Reye's syndrome (4) behavioral deficits in newborn (5) immunotoxin (6)	immediate toxicity: birds: medium to very high (7) fish: medium (8) crustaceans: very high (8) aquatic insects: very high (8) bees: very high (9) aquatic worms: medium (10) water: "practically insoluble" slightly volatile

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
contaminant(s):						
p-nitro-m-cresol						
O,O,S-trimethyl phosphorothioate				oral: high (1)	delayed toxicity (1)	
O,S,S-trimethyl phosphorodithiote				oral: very high (1)	immunotoxin (1)	
fenoxaprop-ethyl Acclaim; Excel; Furore; Option; Whip (±)-ethyl 2-[4-[(6-chloro-2-benoxazolyl) oxy]phenoxy] propanoate CAS # 66441-23-4	miscel-laneous	herbicide	non-pers (1,2)	oral: low to medium (3,4) dermal: ? inhalation: high (3)	teratogen (5)	immediate toxicity: birds: low to medium (2) fish: medium to high (3) crustaceans: medium (3) water: insoluble non-volatile "flammable"
fenpropathrin Danitol; fenpropathrine; Herald; Kilumal; Meothrin; Ortho Danitol; Rody; S-3206; SD 41706; Sumimik; Sumimix (with fenitrothion); Viktor (with clofentizine); WL 41706; XE 938 (*RS*)-α-cyano-3-phenoxybenzyl 2,2,3,3-tetramethylcyclopropanecarboxylate CAS # 64257-84-7	pyrethroid	insecticide	non-pers (1,2)	oral: high (3) dermal: ? inhalation: ?	immunotoxin (4)	immediate toxicity: birds: medium (3) fish: very high (3) water: insoluble slightly volatile
fenthion BAY 29493; Baycid; Bayer 4895; Baytex; DMPT; Ekalux; Entex; Lebaycid; mercaptophos; Quelatox; Queletox; S 1752; Spotton; Talodex; Tiguvon *O,O*-dimethyl-*O*-[4-methylthio]-*m*-tolyl phosphorothioate; phosphorothioic acid *O,O*-dimethyl *O*-3-methyl-4-(methylthio)phenyl CAS # 55-38-9	organo-phosphate	insecticide acaricide avicide restricted use, USA	non-pers (1,2)	oral: medium to high (3) dermal: high (4) inhalation: ?	suspect carcinogen (5) delayed neurotoxin (6) suspect embryotoxin (7) neuromuscular dysfunction (8) eye damage (9,10)	immediate toxicity: birds: very high (11) fish: medium (3,12) crustaceans: high to very high (12) bees: very high (14) aquatic insects: very high (13) water: slightly soluble slightly volatile
transformation product(s):						
sulfoxide analogue of fenthion				oral: high (1)		
sulfone analogue of fenthion				oral: high (1) thirty-six times more toxic than fenthion (2)		

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
fenvalerate Ectrin; Extrin; Fenkill; fenvalethrin; Mikantop (with dimethoate); Moscade; OMS 2000; Pydrin; Pyrid; S-5602; Sanmarton; Sumibac; Sumicidin; Sumicombi (with fenitrothion); Sumifleece; Sumifly; Sumitomo (with fenitrothion); Sumittick; Tirade; WL 43775 (*RS*)-α-cyano-3-phenoxybenzyl (*RS*)-2-(4-chlorophenyl)-3-methylbutyrate CAS # 51630-58-1	pyrethroid	insecticide	mod-pers (1)	oral: ? dermal: ? inhalation: ?	cumulative (2) suspect mutagen (3)	immediate toxicity: birds: low (1) fish: low to very high (1,4) marine invertebrates: high to very high (1) long-term toxicity: fish: adverse effects in gill structure (5) water: insoluble non-volatile to slightly volatile
ferbam Black Fungicide; Carbamate; Coromate; ferbame (France); Ferbert; Fermate; Fermocide; Ferradow; Green Cross kerbam; Hexaferb; Karbam Black; Knockmate; Miller Blue Mold Dust; New Leaf Black Fungicide; Niagar Carbamate; Planters Blue Mold Dust; Sup'r-Flo Ferbam Flowable; Trifungol; Vancide FE 95 iron tris(dimethyldithiocarbamate); ferric dimethyldithiocarbamate CAS # 14484-64-1	thiocar-bamate	fungicide	non-pers (1)	oral: low to medium (2) dermal: ? inhalation: ?	suspect mutagen (3,4) suspect fetotoxin (4,6) kidney damage (5) sperm damage (7)	immediate toxicity: fish: medium to high (1) bees: low to medium (8) long-term toxicity: birds: affects fertility (9) fish: blindness and fin erosion (1); embryotoxic (10) molluscs: "inhibits shell growth" (1) plants: inhibits germination of pollen in some plants (10) water: soluble non-volatile to slightly volatile
transformation product(s): **carbon disulfide** (see carbon disulfide)						
N-nitrosodimethylamine				oral: very high (1)	carcinogen (2,3) mutagen (1,3) liver damage (1)	long-term toxicity: molluscs: may cause reproductive & gastrointestinal damage (4) water: "soluble" oil: "soluble" "volatile" "nonflammable"
fluchloralin BAS-392-H; Basalin *N*-(2-chloroethyl)-α,α,α-trifluoro-2,6-dinitro-*N*-propyl-*p*-toluidine; *N*-(2-chloroethyl)-2,6-dinitro-*N*-propyl-4-(trifluoromethyl)aniline; *N*-(2-chloroethyl)-2,6-dinitro-*N*-propyl-4-(trifluoromethyl)benzenamine CAS # 33245-39-5	dinitro-aniline	herbicide	?	oral: low to medium (1,2) dermal: ? inhalation: medium (2)	?	immediate toxicity: birds: low to medium (2) fish: very high (2) water: slightly soluble slightly volatile to volatile flammable

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
flufenoxuron Cascade; WL 115110 1-[4-(2-chloro-*α,α,α*-trifluoro-*p*-tolyloxy)-2-fluorophenyl]-3-(2,6-difluorobenzoyl)urea; *N*-[[[4-(2-chloro-4-(trifluoromethyl)phenoxy]-2-fluorophenyl]amino]carbonyl]-2,6-difluorobenzamide CAS # 101463-69-8	urea	insecticide	non-pers to mod-pers (1)	oral: low to medium (1) dermal: low to medium (2) inhalation: medium (1)	?	immediate toxicity: birds: low to medium (1) fish: low (1) water: insoluble non-volatile
fluvalinate Klartan; Mavrik; Spur (*RS*)-α-cyano-3-phenoxybenzyl (*R*-2-(2-chloro-*α,α,α*-trifluoro-*p*-toluidino)-3-methylbutyrate CAS # 69409-94-5	pyrethroid	insecticide acaricide	non-pers to mod-pers (1)	oral: high (2) dermal: low (2) inhalation: ?	?	immediate toxicity: birds: low (1) fish: medium to high (1) freshwater invertebrates: low to medium (1) water: insoluble non-volatile to slightly volatile
fosetyl-al Aliette; Aliette Extra (with captan & thiabendazole); Mikal (with folpet); Rhodex (with mancozeb) aluminum tris (o-ethylphosphonate) CAS # 39148-24-8	organo-phosphate	fungicide	more persistent on foliage than in soil (1)	oral: low (1) dermal: ? inhalation: ?	suspect carcinogen (1) degenerative effecst on testes (1) delayed fetal development (1) changes in urinary tract development (1)	immediate toxicity: birds: low (2) fish: low (2) bees: low (1) water: soluble non-volatile

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
glyphosate CP67573; Fallow Master (with dicamba); Landmaster (with 2,4-D); Mon 0573 *N*-(phosphonomethyl)glycine CAS # 1071-83-6	organo-phosphate	herbicide	mod-pers (1,2)	oral: medium (3,4) dermal: medium (3) inhalation: ?	suspect carcinogen (4) suspect mutagen (5)	immediate toxicity: birds: low (6) fish: low to medium (6) crustaceans: low to medium (7) bees: low (6) long-term toxicity: plants: mutagen (8) water: soluble oil: insoluble non-volatile
salt(s): **glyphosate trimesium** Touchdown CAS # 81591-81-3						
isopropylamine salt of glyphosate Pondmaster; Rattler; Rodeo; Roundup; Roundup L&G; Shackle; Shacklet C; Spasor; Sting; Vision *N*-(phosphomethyl)glycine, isopropylamine salt CAS # 38641-94-0						
sodium salt of glyphosate Palado *N*-(phophonomethyl)glycine, sodium salt CAS # 70393-85-0						
transformation product(s): **formaldehyde** (see formaldehyde)						
***N*-nitrosoglyphosate** (in contact with nitric acid)			mod-pers (1)		suspect carcinogen (1) suspect mutagen (1)	
surfactant: **polyoxyethyleneamine**				"LD_{50} of POEA is less than 1/3 that of....(glyphosate)" (1)		immediate toxicity: fish: medium to high (2,3)
contaminant of surfactant: **1,4-dioxane** *p*-dioxane CAS # 123-91-1					carcinogen (1)	

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
lindane Aficide; Agrocide; Asparasin; BBH; Bexol; Borer Kill; Detox 25; Forlin; gamma isomer of BHC; gamma-BHC; gamma-HCH (Gr. Britain); Gammaspra; Gammcide; Gexane; Isotox; Jacutin; Kwell; Lindagam; Lindaterra; Lintox gamma isomer of benzene hexachloride; 1,2,3,4,5,6-hexachlorocyclohexane CAS # 58-89-9	organo-chlorine	insecticide cancelled, most uses, USA, 1983	pers (1)	oral: high to very high (2) dermal: high (2) inhalation: ?	cumulative (2,3) carcinogen (4,5) suspect mutagen (2) teratogen (2) hormone damage (6) testicular damage (7) immunotoxin (2,8) neurotoxin (9,10) aplastic anemia (11) bone marrow damage (12)	BIOACCUM immediate toxicity: birds: medium to high (13) fish: very high (14) amphibians: medium (15) crustaceans: very high (14) earthworms: low (15) aquatic worms: high (16) bees: very high (17) toxic to some plants and phytoplankton (15) long-term toxicity: birds: reduced egg production; eggshell thinning (19) fish: liver damage, behavioral changes (20) amphibians: teratogen (21) plants: mutagen (18) water: slightly soluble oil: "slightly soluble" slightly volatile combustible
transformation product(s): **hydrogen chloride** hydrochloric acid hydrogen chloride CAS # 7647-01-0				oral: low (1)		
2,4,6-trichlorophenol (see 2,4,6-trichlorophenol)						
benzene (see benzene)						
pentachlorobenzene CAS # 608-93-5				oral: high (1)	cumulative (1)	
pentachlorophenol (see pentachlorophenol)						
phosgene gas (see carbon tetrachloride)						

Source: Rachel Carson Council Inc. USA

Factsheets on Pesticides

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
malathion AC 4049; Carbofos; Cythion; Cyuthion; EmmatosAC 4049; For-Mal; Fyfanon; Kop-Thion; Kypfos; Malagram; Malakill; Malamar; Malaphos; Malatal; Malathiozoo; Malaude; Malmed; mercaptothion (South Africa); MLT; Zithiol *O,O*-dimethyl *S*-(1,2-dicarbethoxyethyl) dithiophosphate; *O,O*-dimethyl dithiophosphate of diethyl mercaptosuccinate CAS # 121-75-5	organo-phosphate	insecticide	non-pers (1)	oral: medium to high (2) dermal: medium to high (2) inhalation: medium (2)	suspect mutagen (3) suspect teratogen (4) delayed neurotoxin (5) allergic reactions (6) behavior effects (5) ulcers, gastrointestinal inflammation (7) damage to eyesight (8) abnormal brain waves (9) immunosup-pression (10)	BIOCIDE immediate toxicity: birds: medium to high (11) fish: medium to high (12) bees: very high; nectar of treated plants toxic (13) amphibians: very high (12) crustaceans: medium to very high (12) aquatic worms: medium (13) earthworms: high (12) aquatic insects: very high (12) water: soluble oil: "limited solubility in petroleum oils" slightly volatile to volatile flammable
mancozeb Acarie; Blecar MN; Crittox MZ; Delsene MX 200 (with carbendazim); Dithane M-45; Fore; FT 2M (with Bordeaux mixture); Fubol (with metalaxyl); Furado; Galben (with benalaxyl); Galben M (with benalaxyl); Mancobleu (with copper oxychloride); Manzate 200; manzeb; Manzin; Mycodifol MZ (with folpet); Rhodex (with fosetyl-al); Tedane Extra (with dicofol & dinocap); Turbair Dicamate (with zineb); Vondozeb zinc ion & manganese ethylene bisdithiocarbamate CAS # 8018-01-7	thiocar-bamate	fungicide cancelled, most products, USA	non-pers to mod-pers (1,2)	oral: low (1) dermal: low to medium (3) inhalation: ?	?	immediate toxicity: birds: low to medium (2) bees: low (4) fish: high to very high (2) long-term toxicity: plants: inhibits germination of pollen in some plants (5) water: slightly soluble combustible
transformation product(s): **ethylene thiourea** (see amobam)						
metalaxyl Apron; Fubol (with mancozeb); Proturf; Ridomil; Ridomil Plus (with copper oxychloride); Subdue *N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl)-alanine methyl ester; *N*-(2-methoxyacetyl)-*N*-(2,6-xylyl)-DL-alani-nate CAS # 57837-19-1		fungicide	mod-pers (1)	oral: medium (2) dermal: low to medium (3) inhalation: ?	?	immediate toxicity: fish: low (2) water: soluble
metaldehyde Antimilace; Ariotox; Bug-geta; Cekumeta; Corry's Slug Death; Halizam; Helarion; Meta; metason; Mifaslug; Namekil; Slug Pellets; Snarol Meal metacetaldehyde; *r*-2,*c*-4,*c*-6, *c*-8-tetramethyl-1,3,5,7-tetroxocane; polymer of acetaldehyde CAS # 108-62-3	aldehyde	molluscicide restricted USA, 1974	non-pers (1)	oral: medium (2) dermal: ? inhalation: ?	spinal damage leading to paralysis in hindquarters (3)	water: soluble flammable

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
methomyl S-methyl N-[(methylcarbamoyl)oxy] thioacetimidate CAS # 16752-77-5	carbamate	insecticide nematocide some formulations restricted, USA	non-pers to mod-pers (1)	oral: high to very high (2) dermal: medium (3) inhalation: high (4)	mutagen (5) anemia, respiratory damage, hypersensitivity (6) blood damage (6) liver, kidney, spleen, & bone marrow damage (7)	immediate toxicity: birds: very high (8) fish: medium to high (9) crustaceans: high (9) bees: high (10) aquatic insects: very high (9) water: very soluble slightly volatile
transformation product(s): **acetonitrile**				oral: medium (1)	teratogen (2)	flammable
methyl bromide Bedfume; Brom-O-Gas; Brozone; Celfume; Dowfume; Embafume; Fumigant-1; Iscobrome; Kayafume; MeBr; Meth-O-Gas; Pestmaster; Profume; Rotox; Terr-O-Gas (with chloropicrin); Weed Fume bromoethane; monobromomethane CAS # 74-83-9	miscel-laneous	fumigant	non-pers (1,2)	oral: high (3) dermal: ? inhalation: ?	mutagen (4) neurotoxin (5,6) liver & kidney damage (7) brain damage (8)	water: soluble highly volatile nonflammable
methyl parathion Bladen Extra (with parathion); Cekumethion; Defithion; Folimat Combi (with omethoate); Fostox Metil; Gearphos; Kelthane; Kethane Mixte (with dicofol); metafos; Metaphos; Methyl-bladen; Mixte (with dicofol); Neutrion (with tetradifon); Paralindex (with lindane); Parasoufre Acaricide (with dicofol + sulfur); parathion methyl; Partron M; Sylan Methyl (with endosulfan); Taxylone (with phosalone); Tuver Acaricide (with dicofol & ethion); Verfor; Veromite; Viticarb; Wofatox O,O-dimethyl O-p-nitrophenyl phosphorothioate CAS # 298-00-0	organo-phosphate	insecticide some uses restricted, USA	mod-pers to pers (1,2)	oral: very high (3) dermal: high to very high (3) inhalation: very high (3)	mutagen (4,5) fetotoxin (6) retinal & sciatic nerve damage (3) reduced protein synthesis in fetus (7) immunotoxin (8)	BIOCIDE immediate toxicity: birds: very high (9) fish: medium (3) bees: very high (10) crustaceans: very high (3) long-term toxicity: birds: changes breeding behavior, may reduce reproductive capacity (3,11) fish: reduction in sex hormone, may affect reproduction (12); inhibits feeding behavior (13) plants: chromosome damage (14) water: slightly soluble oil: "slightly [soluble] in petroleum oils" slightly volatile
transformation product(s): **para-nitrophenol** *p*-nitrophenol CAS # 100-02-7				oral: medium to high (1) dermal: high (2)		water: "moderately soluble"

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals: Immediate Toxicity (Acute)	Effects on Mammals: Long-Term Toxicity (Chronic)	Adverse effects on other non-target species Physical properties
metolachlor Bicep (with atrazine); Codal (with prometryn); Cotodon (with dipropetryn); Cotoran multi (with fluometuron); Dual; Milocep (with propazine); Pennant; Primagram & Primextra (with atrazine); Primagram (with atrazine); Primextra (with atrazine); Turbo (with metribuzine) 2-chloro-6'-ethyl-*N*-(2-methoxy-1-methylethyl)acet-*o*-toluidide CAS # 51218-45-2	amide	herbicide	non-pers (1)	oral: medium (2) dermal: low to medium (2) inhalation: low to high (2)	suspect carcinogen (4) testicular atrophy (4)	immediate toxicity: birds: low to medium (3) fish: medium (2) water: soluble slightly volatile
transformation product(s): **nitrosamines** (see dinoseb)						
monocrotophos Azodrin; Bilobran; C 1414; Crisodrin; Monocron; Nuvacron; Plantdrin; SD or Shell SD 9129; Susvin; Ulvair dimethyl phosphate of 3-hydroxy-*N*-methyl-*cis*-crotonamide CAS # 919-44-8	organo-phosphate	insecticide cancelled USA, 1988	non-pers (1)	oral: very high (2) dermal: high (1) inhalation: very high (2)	mutagen (3,4)	immediate toxicity: birds: very high (5) fish: low to medium (2) bees: very high (6) long-term toxicity: crustaceans: reproductive damage (7) water: very soluble oil: "slightly soluble" slightly volatile
nicotine Black Leaf 40 (nicotine sulfate); Destruxol Orchid Spray; Emo-Nik; Fumetobac; Mach-Nic; Niagara P.A. Dust; Nic-Dust; Nic-Sal; Nico-Fume; Nicocide; Ortho N-4 & N-5 Dusts; Tendust 1,3-(1-methyl-2-pyrrolidinyl) pyridine CAS # 54-11-5	botanical	insecticide	?	oral: high (1) dermal: high (2) inhalation: ?	?	immediate toxicity: birds: medium (3) long-term toxicity: birds: teratogen (4) water: "soluble" highly volatile
transformation product(s): **N-nitrosonornicotine**					carcinogen (1)	
nuclear polyhedrosis virus Biotrol VHZ; Elcar; Heliothis NPV, (Elcar); Lymantria dispar NVP (Gypcheck); Orgyia pseudotsugata NPV (TM Biocontrol-1) CAS # 240194-80-1	biological	insecticide		"no adverse effects were observed in any acute oral, dermal, inhalation, and intravenous test" (1)		immediate toxicity: "NPV poses a minimal to non-existent risk to nontarget wildlife" (1)
oxadiazon Ronstar; RP 17623 2-*tert*-butyl-4-(2,4-dichloro-5-isopropoxyphenyl)-Δ^2 1,3,4-oxadiazoline-5-one; 3-[2,4-dichloro-5-(1-methylethoxy) phenyl]-5-(1,1-dimethylethyl-1,3,4-oxadizol-2(3*H*)-one CAS # 19666-30-9	miscel-laneous	herbicide	mod-pers (1)	oral: low to medium (2,3) dermal: medium (3) inhalation: low to medium (3,4)	suspect carcinogen (4,5)	immediate toxicity: birds: low to medium (3) fish: low to medium (3) bees: low to medium (6) crustaceans: medium to high (7) water: insoluble slightly volatile combustible

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
oxydemeton-methyl Croneton MR; Dipterex MR; Ecombi (with parathion); Metasystox R *S*-2-ethylsulfinylethyl *O,O*-dimethylphosphorothiote CAS # 301-12-2	organo-phosphate	insecticide	non-pers (1)	oral: very high (2) dermal: very high (3) inhalation: high (2)	mutagen (4) suspect teratogen (5,6) sperm damage (6)	immediate toxicity: birds: high to very high (7) fish: low to medium (8) crustaceans: high (8) bees: high (9) aquatic insects: high (10) water: miscible oil: sparingly soluble slightly volatile
oxyfluorfen Goal; Koltar; RH-2915 2-chloro-α,α,α-trifluro-*p*-tolyl 3-ethoxy-4-nitrophenyl ether CAS # 42874-03-3	miscel-laneous	herbicide cancelled, most products, USA 1982	non-pers (1)	oral: low (1) dermal: low to medium (2) inhalation: ?	suspect mutagen (4) blood, kidney, liver, and thyroid damage (4)	immediate toxicity: birds: low to medium (3) fish: high (3) water: insoluble slightly volatile
contaminant(s): **perchloroethylene** CAS # 127-84-4					carcinogen (1) suspect fetotoxin (1)	
paradichlorobenzene Di-chloride; Para Crystals; Para Nuggets; Paracide; Paradow; Paramoth 1,4-dichlorobenzene; *p*-dichlorobenzene CAS # 106-46-7	organo-chlorine	fumigant	?	oral: medium (1) dermal: ? inhalation: ?	suspect carcinogen (2) suspect mutagen (3) liver & kidney damage (2,3) lung damage (2) anemia (2)	immediate toxicity: fish: medium (4) long-term toxicity: plants: mutagen (3) water: slightly soluble oil: "lipophilic" highly volatile

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
paraquat Actor (with diquat); Cyclone (with diquat); Dexuron (with diuron); Farmon PDQ (with diquat); Gramazine (with simazine); Gramixel (with diuron); Gramuron (with diuron); Groundhog (with amitrole & diquat & simazine); methyl viologen; Pardi-Weedol (with diquat); Pathclear (with amitrole & diquat & simazine); Preglone (with diquat); Reglox (with diquat); Soltair (with diquat & simazine); Spraygrow (with diquat); Sprayseed (with diquat); Spraytop (with diquat); Surefire (with diuron); Talent (with asulam); Totacol (with diuron) 1,1'-dimethyl-4,4'-bipyridinium CAS # 4685-14-7	bypiridyl	herbicide voluntary withdrawal from market, Norway, 1981 banned in Sweden, 1983 Banned in Netherlands, 1989	non-pers (1,2)	oral: high to very high (3) dermal: very high (3) inhalation: high (3)	suspect mutagen (4) suspect teratogen (5) suspect neurotoxin (6) fingernail loss (7) liver, kidney, pancreas, gastrointestinal tract, adrenal, nerve, brain, heart, muscle and eye damage (6,8) irreversible lung injury within hours of ingestion (7) implicated in Parkinson's disease (9,10)	immediate toxicity: birds: high fish: low to medium (2,11) amphibians: low (2) crustaceans: low to medium (2) aquatic insects: low (11) microorganisms: toxic to some (12) long-term toxicity: birds: embryotoxin (13); growth rate, adverse effects; blood damage (14,15) amphibians: clinical syndrome of Parkinson's disease (9) blue-green algae: mutagen (16) water: "soluble"
related compound(s): **emetic** (formulated into technical paraquat in case of ingestion)					heart damage (1)	
transformation product(s): **formaldehyde** (see formaldehyde)						
paraquat dichloride Dextrone (with diquat); Galgo-quat; Gramonol (with monolinuron); Gramoxone (with MCPA); Gramoxone Special; Liro-paraquat; Longlife Plus; Ortho paraquat; Prelude; Protex; R-Bix; Radex; Scythe; Sipquat; Speedway; Sweep; Terraklene (with simazine); Violan 1,1'-dimethyl-4,4'-bypiridinium dichloride CAS # 1910-42-5	bypiridyl	herbicide dessicant defoliant plant growth regulator		oral: high to very high (1,2) dermal: high (3) inhalation: very high (4) many long-term symptoms may begin immediately from single or minimal exposure (see long-term toxicity)	suspect carcinogen (4) suspect mutagen (4) brain damage (5)	immediate toxicity: birds: medium to high (6) fish: low to medium (1) crustaceans: medium to high (4) long-term toxicity: birds: egg hatchability, adverse effects (3) amphibians: teratogen (7) water: "soluble" "non-volatile"
transformation product(s): **QINA**						

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use, Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
PCBs Arochlor; Chlophen; Chlorextrol; Clophen; Dykanol; Fenchlor; Inerteen; Kanechlor; Nollamol; Phenochlor; Pyralene; Pyranol; Sentotherm; Therminol polychlorinated biphenyls chlorinated biphenyls chlorinated diphenyls The total number of PCB's is over 200 half of which are commonly found among the commericial preparations. CAS # 1336-36-3	organo-chlorine	formerly used to reduce vapor pressure and prolong residual activity of pesticides cancelled, all products, USA, 1970	pers (1)	oral: low to medium (2)	cumulative (3) carcinogen (4) immunotoxin (5) liver damage (2) neurotoxin (6) decreased homoglobin (1) chloracne (2) reduced fertility (7)	BIOCIDE immediate toxicity: fish: low to high (8) crustaceans: medium to very high (8) bees: low to medium (9) long-term toxicity: birds: behavioral defecits; reduced egg shell thickness. (10,11) biomagnification (1) water: insoluble oil: soluble slightly volatile to volatile "nonflammable"
contaminant(s): **pentachlorodibenzofuran**	dibenzo-furan					
chlorinated naphthalenes					chloracne (1) liver damage (1) hyperkeratosis (1)	
tetrachlorodibenzofuran	dibenzo-furan					
pendimethalin AC 92553; Accotab; Go-Go-San; Herbadox; Horbadox; Prowl; Sipaxol; Squadron (with imazaquin); Stomp; Way Up 2,6-dinitro-3,4-xylidine CAS # 40487-42-1	dinitro-aniline	herbicide	non-pers to mod-pers (1)	oral: medium (2,3) dermal: low to medium (3) inhalation: low (3)	?	immediate toxicity: fish: high (4) birds: low (2) crustaceans: high (4) water: insoluble oil: very soluble slightly volatile flammable
transformation product(s): ***N*-nitrosopendimethalin** *N*-(1-ethylpropyl)-*N*-nitroso-3,4-dimethyl-2,6-dinitrobenzamine			mod-pers (1)	oral: ? dermal: ? inhalation: ?		
permethrin Ambush; Atroban; Bio Flydown; Corsair; Dragon; Ectiban; Expar; Gard-Star; Hard-Hitter; Insectiban; Jureong; Kafil; Nix; Over-Time; Permectrin; Pounce; Quamlin; Rondo; Stockade; Tornade; Torpedo 3-phenoxybenzyl (1*RS*)-*cis,trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropanecarboxylate CAS # 52645-53-1	pyrethroid	insecticide acaricide	non-pers (1)	oral: low to high (2) dermal: ? inhalation: low to high (3)	blood damage (4)	immediate toxicity: fish: very high (5) birds: "practically non-toxic" (2) marine invertebrates: very high (6) bees: "toxic" (7) water: insoluble to slightly slightly soluble non-volatile combustible

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
phorate AAstar (with flucythrinate); Corliss (with terbufos); Cygard (with terbufos); Geomet; Granutox; Thimet *O,O*-diethyl *S*-ethylthiomethyl phosphorodithiote CAS # 298-02-2	organo-phosphate	insecticide restricted use, USA	non-pers (1)	oral: very high (2) dermal: very high (2) inhalation: very high (1)	mutagen (3)	immediate toxicity: birds: very high (4) fish: very high (5) amphibians: high (4) crustaceans: very high (5) bees: medium (6) aquatic insects: very high (5) water: slightly soluble volatile
phosalone Azofene; Benzphos; Fozalon; NIA-9241; NPH-1091; phosalon; Ranbeck (with dichlorvos); Ransbeck (with dichlorvos); RP 11974; Rubitox; Taxylone (with methyl parathion); Zolone; Zolone Flo; Zolone Liquid *S*-6-chloro-2,3-dihydro-2-oxo-1,3-benzoxazol-3-ylmethyl *O,O*-diethyl phosphorodithioate CAS # 2310-17-0	organo-phosphate	insecticide acaricide	non-pers (1)	oral: high (2) dermal: high (2) inhalation: ?	?	immediate toxicity: birds: high (1) fish: high to very high (3) crustaceans: very high (4) bees: high (5) oil: "insoluble" non-volatile
phosphamidon Apamidon; Dimecron 2-chloro-2-diethylcarbamoyl-1-methylvinyl dimethyl phosphate; 2-chloro-3-dimethoxyphosphinoyloxy-*N,N*-diethylbut-2-enamide CAS # 13171-21-6	organo-phosphate	insecticide, acaricide restricted use, USA	?	oral: very high (1) dermal: very high (1) inhalation: high (2)	mutagen (3) embryotoxin (4) testicular damage (5) liver damage (6)	BIOCIDE immediate toxicity: birds: very high (7) fish: medium to high (8) crustaceans: very high (8) aquatic insects: very high (8) long-term toxicity: birds: "teratogenic" (9) water: very soluble slightly volatile
pirimiphos-methyl Actellic; Actellifog; Attack (with permethrin); Blex; Cyperallic (with cypermethrin); Giustiziere; Pirigrain; PP-511; Silo-San; Silosan; Singsing (with cypermethrin); Sybol 2 *O*-[2-(diethylamino)-6-methyl-4-pyrimidinyl] *O,O*-dimethylphosphorothioate; 2-dimethylamino-6-methylpyrimidin-4-yl dimethyl phosphorothioate CAS # 29232-93-7	organo-phosphate	insecticide, acaricide	non-pers (1)	oral: medium (2) dermal: medium to high (3) inhalation: ?	mutagen (4)	immediate toxicity: birds: high to very high (5) fish: "toxic" (5) water: slightly soluble volatile
propanil Trio (with bromoxynil & 2,4-D) *N*-(3,4-dichlorophenyl) propanamide CAS # 709-98-8	amide	herbicide restricted use, USA	non-pers (1)	oral: medium (2) dermal: medium (1) "should not be breathed or allowed to get in eyes or on skin" (1)	methemo-globinemia (2) hemolytic anemia (3)	immediate toxicity: birds: high (4) fish: medium (5) crustaceans: medium (4) long-term toxicity: birds: suspect teratogen (6) bees: low to medium (7)
components: **tetrachloroazoxy benzene**						water: soluble slightly volatile

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
propanil Trio (with bromoxynil & 2,4-D) *N*-(3,4-dichlorophenyl) propanamide CAS # 709-98-8	amide	herbicide restricted use, USA	non-pers (1)	oral: medium (2) dermal: medium (1) "should not be breathed or allowed to get in eyes or on skin" (1)	methemo-globinemia (2) hemolytic anemia (3)	immediate toxicity: birds: high (4) fish: medium (5) crustaceans: medium (4) long-term toxicity: birds: suspect teratogen (6) bees: low to medium (7)
components: **tetrachloroazoxy benzene**						water: soluble slightly volatile
3,3,4,4 tetrachloroazobenzene					chloracne and hyperkeratosis (1) liver damage (2)	
propoxur aprocarb; arprocarb; BAY 39007; Baygon Spray (with dichlorvos & cyfluthrin); Blattanex Residual Spray (with dichlorvos); Boygon; Brygou; Chemagro 9010; Isocarb; o-IMPC; PHC; Raid Ant & Roach Killer; Raid Wasp & Hornet Killer; Sendran; Suncide; Tat Ant Trap; Unden o-isopropoxyphenyl-*N*-methyl carbamate; 2-(1-methylethoxy)phenol methyl carbamate CAS # 114-26-1	carbamate	insecticide	mod-pers (1)	oral: very high (2) dermal: medium to high (2) inhalation: ?	carcinogen (3,4) suspect mutagen (5) learning disability (6)	BIOCIDE immediate toxicity: birds: very high (7) fish: high (8) bees: high (11) amphibians: medium (9) crustaceans: very high (9) aquatic insects: very high (9) aquatic worms: very high (10) long-term toxicity: toxic to some plants (12) water: soluble slightly volatile
transformation product(s): **n-nitroso propoxur**					mutagen (1)	long-term toxicity: plants: mutagen (2)
pyrethrum "Insect powder" *Chrysanthemum cinaeraraefolum*; mixture of pyrethrin I & II, cinerin I & II, jasmolin I & II	botanical	insecticide	non-pers (1)	oral: medium to high (1,2) dermal: ? inhalation: ?	liver damage, especially with synergists and Freon propellant (3) allergic reactions (4) neurotoxin (4)	immediate toxicity: birds: low (5) fish: very high (6) crustaceans: very high (6) water: "not soluble in water" oil: "100% in petroleum distillate" combustible
simazine Amizine (with amitrole); Aquazine; Batazina; CDT; CET; Framed; Gesatop; Herbazin; Herbex; Herbox; Herboxy; Hungazin DT; Premazine; Primatol S; Princep; Printop; Radocon; Simadex; Zeapur 2-chloro-4,6-bis(ethylamino)-*s*-triazine CAS # 122-34-9	triazine	herbicide soil sterilant	mod-pers to pers (1,2)	oral: low to medium (3,4) dermal: low to medium (4) inhalation: low to medium (4)	testes, kidneys, liver & thyroid damage (5) disturbances in sperm production (5)	immediate toxicity: birds: low (6) fish: low to medium (4) crustaceans: low (4) molluscs: low to high (4) bees: low (7) aquatic insects: medium to high (6) water: slightly soluble oil: slightly soluble non-volatile "nonflammable"

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
sodium cyanide Cymag; M-44 devices hydrocyanic acid, sodium salt CAS # 143-33-9	cyanide	fumigant insecticide rodenticide cancelled most uses, USA, 1988	?	oral: very high dermal: ? inhalation: ?	?	?
transformation product(s): **hydrogen cyanide** (see hydrogen cyanide)						
streptomycin *O*-2-deoxy-2-methylamino-*α*-L-glucopyranosyl-(1→2)-*O*-5-deoxy-3-*C*-formyl-*α*-L-lyxofuranosyl-(1→4)-N^3,N^3-diamidino-D-strepamine CAS # 57-92-1	antibiotic	antibiotic, fungicide		oral: low (1) dermal: ? inhalation: ?	ear damage (2)	water: very soluble
strychnine strychinidin-10-one CAS # 57-24-9	botanical	rodenticide, avicide most uses cancelled, USA by 1988	"stable in the enviornment" (1)	oral: very high (2) dermal: ? inhalation: "do not inhale" (3)		immediate toxicity: birds: very high (1) amphibians: very high (2) long-term toxicity: secondary poisoning water: slightly soluble "nonflammable"
sulfur Bolda (with maneb & carbendazim); brimstone; Colsul; Corosul D and S; Cosan; flour sulfur; flowers of sulfur; Hexasul; Kolo-100 (with dichlone); Kolofog; Kolospray; Kumulus S; Magnetic 70, 90 and 95; precipitated sulfur; Sofril; Spersul; Sulforon; Sulkol; Thiolux; Thiovit sulfur CAS # 7704-34-9	metal/ mineral sulfur	fungicide acaricide	perm	oral: low (1) dermal: high (1) inhalation: low to medium (1)	?	immediate toxicity: birds: low (1) fish: low (1) estuarine/marine organisms: low (1) aquatic invertebrates: low (1) water: "insoluble"
compound(s): **sulfuryl fluoride** sultropene (France); Vikane CAS # 2699-79-8	metal/ mineral sulfur	fumigant restricted use, USA, all formulations		oral: high (1) inhalation: medium (1)	liver and kidney damage (2) mottled teeth (2) osteosclerosis (3)	immediate toxicity: plants: toxic to some (1) water: soluble highly volatile
temephos Abat; Abate; Abathion; Abazan (with trichlofon); AC 52160; Biothion; Difenthos; Nimitex; Nimitox; Swebate; temophos *O,O,O′,O′*-tetramethyl *O,O′*-thiodi-*p*-phenylene phosphorothioate; *O,O′*-(thio-4,1-phenylene)bis[*O,O*-dimethyl phosphorothioate] CAS # 3383-96-8	organo-phosphate	insecticide	non-pers (1)	oral: low to medium (2,3) dermal: medium (4) inhalation: ?	liver damage (3)	immediate toxicity: birds: high to very high (5) fish: low to high (6) amphibians: low to medium (5) crustaceans: very high (7) aquatic insects: very high (6) bees: high (8) water: insoluble

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
thiophanate methyl Cercobin M; Ditek; Fungo; Hitrun (with vinclozolin); Labilite; Mildothane; NF-44; TD-1881; Thiophanate M; Topsin M; Zyban dimethyl[1,2-phenylene)bis (iminocarbonothioyl)] bis[carbamate]; dimethyl 4,4'-o-phenylenebis (3-thioallophanate); bis[3-(methoxycarbonyl)-2-thioureido]benzene CAS # 23564-05-8	carbamate	fungicide	non-pers (1)	oral: low (2) dermal: low to medium (3) inhalation: low to medium (3)	decreased body weight of newborn (4)	immediate toxicity: birds: low (3) fish: medium to high (3) earthworms: very high (5) water: "insoluble"
transformation product(s): **carbendazim** (see carbendazim)						
thiram Accelerator Thiuram; Aules Chipco Thiram 75; Cyuram DS; Deksan; Ekagom TV; Fernasan; Hexthir; Mercuram; Nobencutan; Panoram; Pomarsol Forte; Royal TMTD; Spotrete; Thioknock; Thirasan; Trameton; Tripomol; Tuads; Tues; Tulisan; Vulkacit MTIC bis(dimethylthiocarbamoyl)disulfide; tetramethylthiuram disulfide; tetramethylthiperoxydicarbonic diamide CAS # 137-26-8	thiocarbamate	fungicide animal repellent	non-pers (1)	oral: medium (2) dermal: ? inhalation: low to high (3) avoid alcohol ingestion before or after exposure (see disulfiram) (14)	cumulative (4) suspect mutagen (5,6) teratogen (7,8) liver damage (9,10)	immediate toxicity: birds: medium to high (3) fish: medium to high (3) bees: medium (11) long-term toxicity: birds: excess build-up of cartilage in legs (12); reproductive damage (13) plants: suspect mutagen (8) water: slightly soluble
related compound(s): **disulfiram** Antabuse; deters alcohol ingestion; ethyl analogue of thiram tetraethylthiuram disulfide				neurological effects; 10 times less toxic than thiram (1)	suspect teratogen (1,2) liver damage (1)	
transformation product(s): **N-nitrosodimethylamine** (see ferbam)						
triallate Buckle (with trifluralin); CP 23426; DATC-BW; Far-Go; tri-allate	thiocarbamate	herbicide	mod-pers (1)	oral: medium (2) dermal: low to medium (1) inhalation: ?	suspect carcinogen (3) suspect mutagen (4) suspect neurotoxin (3)	immediate toxicity: birds: low to medium (1) fish: high (2) crustaceans: high (2) bees: low to medium (6)

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
triallate (*cont.*) *S*-2,2,3-trichloroallyl di-isopropylthiolcarbamate CAS # 2303-17-5					brain, liver, and spleen damage (5)	long-term toxicity: birds: liver, kidney, and reproductive damage; (7) delayed neurotoxicity (3) water: slightly soluble volatile "nonflammable"
triazophos Deltaphos (with deltamethrin); Hostathion *O,O*-diethyl *O*-1-phenyl-1*H*-1,2,4-triazol-3-yl phosphorothiote CAS # 24017-47-8	organo-phosphate	insecticide	mod-pers (1)	oral: high (2) dermal: low to medium (2) inhalation: ?	suspect mutagen (3)	immediate toxicity: birds: very high (4) fish: medium (4) water: slightly soluble slightly volatile
trichlorfon Anthon; BAY L 13/59; Bovinox; Briten; Cekufon; chlorofos (USSR); Ciclosam; Danex; Denkaphon; Dipterex; Diptetes; Ditrifon; Equino-Acid; Leivasom; metrifonate; Neguvon; Proxol; trichlorofon; Trinex; Tugon dimethyl (2,2,2-trichloro-1-hydroxyethyl)-phosphonate CAS # 52-68-6	organo-phosphate	insecdticide	mod-pers (1)	oral: high (2) dermal: low to medium (2) inhalation: low to high (3)	suspect carcinogen (4,5) suspect mutagen (4,7) suspect teratogen (4) fetotoxin (8) bone marrow & liver damage(4,9) immunotoxin (10)	BIOCIDE immediate toxicity: birds: high to very high (11) fish: medium to high (12) aquatic insects: very high (12) crustaceans: medium to very high (12) aquatic worms: very high (13) bees: medium (14) long-term toxicity: plants: suspect mutagen (15) water: very soluble oil: "insoluble" slightly volatile
transformation product(s): **dichlorvos** (see dichlorvos)						
trifluralin Buckle (with triallate); Cannon (with alachlor); Carpidor; Commence (with clomazone); Ipersan; Janus; Laurel; Lextra (with linuron); Mudekan; Salute (with metribuzin); Su Seguro Cardidor; Trefanocide; Treficon; Treflan; trifluraline (France) *α,α,α*-trifluoro-2,6-dinitro-*N,N*-dipropyl-*p*-toluidine CAS # 1582-09-8	dinitro-aniline	herbicide cancelled, most uses, USA, 1982	mod-pers (1,2)	oral: low (3) dermal: low to medium (4) inhalation: ?	suspect carcinogen (5,6) suspect mutagen (7,8) suspect teratogen (9) fetotoxin (5)	immediate toxicity: birds: low (5) fish: high to very high (10) amphibians: very high (11) crustaceans: high to very high (10) bees: low to medium (12) aquatic insects: medium (10) water: insoluble volatile
contaminant(s): ***N*-nitroso-di-*n*-propylamine**				oral: high (1)	carcinogen (2,3) mutagen (4,5)	

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
trifluralin Buckle (with triallate); Cannon (with alachlor); Carpidor; Commence (with clomazone); Ipersan; Janus; Laurel; Lextra (with linuron); Mudekan; Salute (with metribuzin); Su Seguro Cardidor; Trefanocide; Treficon; Treflan; trifluraline (France) α,α,α-trifluoro-2,6-dinitro-*N*,*N*-dipropyl-*p*-toluidine CAS # 1582-09-8	dinitro-aniline	herbicide cancelled, most uses, USA, 1982	mod-pers (1,2)	oral: low (3) dermal: low to medium (4) inhalation: ?	suspect carcinogen (5,6) suspect mutagen (7,8) suspect teratogen (9) fetotoxin (5)	immediate toxicity: birds: low (5) fish: high to very high (10) amphibians: very high (11) crustaceans: high to very high (10) bees: low to medium (12) aquatic insects: medium (10) water: insoluble volatile
contaminant(s): **N-nitroso-di-*n*-propylamine**				oral: high (1)	carcinogen (2,3) mutagen (4,5)	
warfarin Arab Rat Deth; coumafene (France); Dethmor; Eastern States Duocide; Fasco Fascrat Powder; Fatal; Kypfarin; Martin's Mar-Frin; Rat & Mice Bait; Rat Gard; Rat-Death; Rat-Kill; Rat-Mix; Rat-Nix; Rat-O-Cide; Rat-Ola; Rataway; Twin Light Rat Away; Warfarat; zoocoumarin (USSR & Netherlands) 3-(α-acetonylbenzyl)-4-hydroxycoumarin CAS # 81-81-2	coumarin	rodenticide	?	oral: high (1) dermal: ? inhalation: ?	teratogen (2,3)	water: slightly soluble slightly volatile
zinc phosphide Gopha-Rid; idall-Zinc; Kilrat; Mole and Gopher Bait; Mouse-con; Phosvin; Rodent Pellets; Rumetan zinc phosphide CAS # 1314-84-7	metal/ mineral zinc	insecticide rodenticide restricted use, USA "confined, in many countries, to trained personnel"	non-pers "under exposed acid-free conditions will remain active for long periods of time" (1) "stable when dry" (2)	oral: very high (1) dermal: ? inhalation: ? "do not inhale, avoid skin contact" (3)	?	immediate toxicity: birds: very high (4) fish: "negligible" (5) crustaceans: "in stream killed many" (6) water: insoluble
transformation product(s): **phosphine gas** (see aluminum phosphide)						

Source: Rachel Carson Council Inc. USA

NAME: Common Trade and Other Chemical CAS Number	Class of Chemical	Chief Pesticide Use; Status	Persistence	Effects on Mammals		Adverse effects on other non-target species Physical properties
				Immediate Toxicity (Acute)	Long-Term Toxicity (Chronic)	
zineb Asporum; Blightox; Blizene; Cineb; Crittox; Crystal Zineb; Hexathane; Kupratsin; Kypzin; Lonacol; Micide; Miltox; Novozin N 50; Parzate; Pomarsol S Forte; Thiodow; Tritofterol; Zebtox; Zidan; Zinosan zinc ethylene bisdithiocarbamate CAS # 12122-67-7	thiocarbamate	fungicide cancelled, most products, USA	non-pers to mod-pers (1)	oral: low (2) dermal: low to medium (3) inhalation: ?	anemia (3)	immediate toxicity: birds: low to medium (4) long-term toxicity: fish: embryotoxin (5) amphibians: teratogen (6) plants: toxic to some; inhibits germination of pollen in some plants (7) water: slightly soluble combustible
transformation product(s): **ethylene thiourea** (see amobam)						
ziram Corozate; Cuman; Fuclasin Ultra; Fuklasin; Hexazir; Karbam; Methasen; Mezene; Milbam; Niagara Z-C Spray; Opalate; Pomarsol Z Fote; Prodaram; Tricarbamix Z; Triscabol; Vancide MZ-96; Z-C Spray; Zerlate; Zincmate; Ziram Technical bis(dimethyldicarbamato)zinc; zinc dimethyl dithiocarbamate CAS # 136-30-4	thiocarbamate	fungicide	non-pers (1)	oral: medium (2) dermal: ? inhalation: ?	suspect carcinogen (3,4) suspect mutagen (3,5) suspect teratogen (6,7) bone damage (8)	immediate toxicity: fish: high (1) bees: "nontoxic" (3) long-term toxicity: birds: reproductive damage (9,10)
transformation product(s): **carbon disulfide** (see carbon disulfide)						
dimethylamine (see dimethylamine)						
N-nitrosodimethylamine (see ferbam)						

Source: Pages 1-37 of this publication are drawn from Basic Guide to Pesticides - Their Characteristics and Hazards by Dr Shirley A. Briggs and the staff of Rachel Carson Council Inc. published in 1993 by Taylor and Francis Washington D.C. USA.

Glyphosate (Roundup)

A factsheet by the Northwest Coalition for Alternatives to Pesticides (NCAP).

• Glyphosate is a broad-spectrum herbicide widely used to kill unwanted plants both in agriculture and in nonagricultural landscapes. Most glyphosate-containing products are either made or used with a surfactant, chemicals that help glyphosate penetrate plant cells.

• Glyphosate-containing products are acutely toxic to animals, including humans. Symptoms include eye and skin irritation, headache, nausea, numbness, elevated blood pressure, and heart palpitations. The surfactant used in a common glyphosate product (Roundup) is more acutely toxic than glyphosate itself; the combination of the two is yet more toxic.

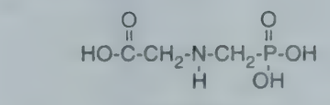
• Given the marketing of glyphosate herbicides as benign, it is striking that laboratory studies have found adverse effects in all standard categories of laboratory toxicology testing. These include medium-term toxicity (salivary gland lesions), long-term toxicity (inflamed stomach linings), genetic damage (in human blood cells), effects on reproduction (reduced sperm counts in rats; increased frequency of abnormal sperm in rabbits), and carcinogenicity (increased frequency of liver tumors in male rats and thyroid cancer in female rats).

• In studies of people (mostly farmers) exposed to glyphosate herbicides, exposure is associated with an increased risk of miscarriages, premature birth, and the cancer non-Hodgkin's lymphoma.

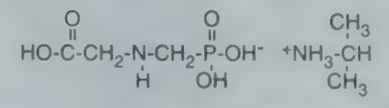
• Glyphosate has been called "extremely persistent" by the U.S. Environmental Protection Agency, and half lives of over 100 days have been measured in field tests in Iowa and New York.

By Caroline Cox

Glyphosate



glyphosate
N-(phosphonomethyl)glycine



isopropylamine salt of glyphosate

Described by their manufacturer as pesticides of "low toxicity and environmental friendliness,"[1] glyphosate-based herbicides can seem like a silver bullet when dealing with unwanted vegetation. However, glyphosate poses a variety of health and environmental hazards.

Glyphosate, N-(phosphonomethyl) glycine, is a systemic and nonselective herbicide used to kill broad-leaved, grass, and sedge species.[2] It has been registered in the U.S. since 1974 and is used to control weeds in a wide variety of agricultural, urban, lawn and garden, aquatic and forestry situations.[3] Most glyphosate herbicides contain the isopropylamine salt of glyphosate.[4] Unlike most other herbicides, chemicals which are closely related to glyphosate are not effective herbicides.[5]

Glyphosate products are manufactured by Monsanto Company worldwide. They are marketed under a variety of trade names: Roundup, Rodeo, and Accord are the most common names in the United States.[2]

Use of glyphosate

Glyphosate is the seventh most commonly used pesticide in U.S. agriculture, the third most commonly used pesticide on industrial and commercial land, and the second most commonly used home and garden pesticide. Estimated annual use according to the U.S. Environmental Protection Agency (EPA) is between 38 and 48 million pounds.[6] The largest agricultural uses are in production of soybeans, corn, hay and pasture, and on fallow land.[7] Glyphosate use is currently (1998) growing at a rate of about 20% annually, primarily because of the recent introduction of crops which are genetically engineered to be tolerant of the herbicide.[8]

Mode of action

Glyphosate's mode of action is "not known at this time,"[1] according to EPA. However, considerable research has established that glyphosate inhibits an enzyme pathway, the shikimic acid pathway, preventing plants from synthesizing three aromatic amino acids. These amino acids are essential for growth and survival of most plants. The key enzyme inhibited by glyphosate is called EPSP synthase.[9] Glyphosate also "may inhibit or repress"[1] two other enzymes, involved in the synthesis of the same amino acids.[4] These enzymes are present in higher plants and microorganisms but not in animals.[9]

Glyphosate can affect plant enzymes not connected with the shikimic acid pathway. In sugar cane, it reduces activity of one of the enzymes involved in sugar metabolism.[10] It also inhibits a major detoxification enzyme in plants.[11]

Roundup affects enzymes found in mammals. In rats, Roundup decreased activity of two detoxification enzymes in the liver and an intestinal enzyme.[12]

"Inert" ingredients in glyphosate-containing products

Virtually every pesticide product contains ingredients other than what is called the "active" ingredient(s), the one designed to provide killing action. These ingredients, misleadingly called "inerts," are added to make the product easier to use or more

Source: Global Pesticide Campaigner, April 1999, Vol. 9, NO. 1. Published by Pesticide Action Network-NA, San Francisco, USA

efficient. In general, they are not identified on the labels of pesticide products.

Many of the toxicology studies that will be summarized in this factsheet have been conducted using glyphosate, the active ingredient, alone. Some have been conducted with commercial products containing glyphosate and "inert" ingredients. When no testing is done with the product as it is actually used, it is impossible to accurately assess its hazards.We will discuss both types of studies and will identify, insofar as is possible, what material was used in each study.

Acute toxicity to laboratory animals

Glyphosate's acute oral median lethal dose (the dose that causes death in 50% of a population of test animals or LD_{50}) in rats is greater than 4,320 milligrams per kilogram (mg/kg) of body weight. This places the herbicide in Toxicity Category III (Caution).[4] Its acute dermal toxicity (dermal LD_{50}) in rabbits is greater than 2,000 mg/kg of body weight, also Toxicity Category III.[4]

Commercial glyphosate herbicides are more acutely toxic than glyphosate alone. The amount of Roundup (containing glyphosate and the surfactant POEA) required to kill rats is about 1/3 the amount of glyphosate alone.[13] Roundup is also more acutely toxic than POEA alone.[13]

Glyphosate-containing products are more toxic via inhalation than orally. Inhalation of Roundup by rats caused "signs of toxicity in all test groups,"[14] even at the lowest concentration tested. These signs included gasping, congested eyes, reduced activity,[15] and body weight loss.[14] Lungs were red or blood-congested.[15] The dose required to cause lung damage and mortality following pulmonary administration of two Roundup products and POEA (when forced into the trachea, the tube carrying air into the lungs) was only 1/10 the dose causing damage orally.[13,16]

Acute toxicity to humans

Acute toxicity of glyphosate products to humans was first publicized by physicians in Japan who studied 56 suicide attempts; nine cases were fatal. Symptoms included intestinal pain, vomiting, excess fluid in the lungs, pneumonia, clouding of consciousness, and destruction of red blood cells.[17] They calculated that fatal cases ingested on average about 200 milliliters (3/4 of a cup). They believed that POEA was the cause of Roundup's toxicity.[17] More recent reviews of poisoning incidents have found similar symptoms, as well as lung dysfunction,[18-20] erosion of the gastrointestinal tract,[18,20]abnormal electrocardiograms,[20] low blood pressure,[18,20] kidney damage,[18,19,21] and damage to the larynx.[22]

Smaller amounts of Roundup cause adverse effects, usually skin or eye irritation as well as some of the symptoms listed above. For example, rubbing of Roundup in an eye caused eye and lid swelling, rapid heartbeat and elevated blood pressure. Wiping the face after touching leaky spray equipment caused swelling of the face. Accidental drenching with horticultural Roundup caused eczema of hands and arms lasting two months.[19] A spill resulted in dizziness, fever, nausea, palpitations and sore throat.[23]

Table 1
Symptoms Following Unintentional Exposure to Glyphosate Herbicides

eye irritation	blisters
painful eyes	skin rash
burning eyes	rapid heartbeat
blurred vision	heart palpitations
swollen eye, face, joints	elevated blood pressure
facial numbness	chest pains
burning sensation on skin	congestion
itchy skin	coughing
tingling skin	headache
recurrent eczema	nausea

Temple, W.A. and N.A. Smith. 1992. Glyphosate herbicide poisoning experience in New Zealand. N.Z. Med. J. *105:173-174.*
Calif. EPA. Dept. of Pesticide Regulation. 1998. Case reports received by the California Pesticide Illness Surveillance Program in which health effects were attributed to glyphosate, 1993-1995. Unpublished report.

Toxicology overview

Glyphosate is often portrayed as toxicologically benign[24]; however, NCAP's review of glyphosate's toxicology comes to a different conclusion. Adverse effects have been identified in each standard category of testing (subchronic, chronic, carcinogenicity, mutagenicity, and reproduction). NCAP's review has been challenged by the assertion that these effects were found because standard test protocols *require* finding adverse effects at the highest dose tested. The following five sections of this article summarize adverse effects that did *not* result from this requirement: they were all found at less than the highest dose tested. (The few exceptions are clearly identified.)

Subchronic toxicity

In subchronic (medium term) studies of rats and mice done by the National Toxicology Program (NTP), microscopic salivary gland lesions were found in all doses tested in rats (200 - 3400 mg/kg per day) and in all but the lowest dose tested in mice (1,000-12,000 mg/kg per day). A follow-up study by NTP found that the mechanism by which glyphosate caused these lesions involved the hormone adrenalin.[25]

The NTP study also found increases in two liver enzymes at all but the two lowest doses tested. Other effects found in at least two doses in this study were reduced weight gain in rats and mice; diarrhea in rats; and changes in kidney and liver weights in male rats and mice.[25] Another subchronic laboratory test found that blood levels of potassium and phosphorus in rats increased at all doses tested (60-1600 mg/kg/day).[4]

Glyphosate-containing products are more toxic than glyphosate in subchronic tests. In a seven day study with calves, 790 mg/kg per day of Roundup caused pneumonia and death of 1/3 of the animals tested. At lower doses decreased food intake and diarrhea were observed.[2]

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Chronic toxicity

Glyphosate is also toxic in long-term studies. At all but the lowest dose tested, excessive cell division in the urinary bladder occurred in male mice[1] and inflammation of the stomach lining occurred in both sexes of rats.[2]

Carcinogenicity

A recent Swedish study of hairy cell leukemia (HCL), a form of the cancer non-Hodgkin's lymphoma, found that people who were occupationally exposed to glyphosate herbicides had a threefold higher risk of HCL. A similar study of people with non-Hodgkin's lymphoma found exposure to glyphosate herbicides was associated with an increase in risk of about the same size.[25a,b]

Publicly available laboratory studies of glyphosate's ability to cause cancer were all conducted by or for its manufacturer.[2] The first carcinogenicity study submitted to EPA (1981) found an increase in testicular tumors in male rats at the highest dose tested as well as an increase in the frequency of a thyroid cancer in females. Both results occurred at the highest dose tested (30 mg/kg of body weight per day).[26,27] The second study (1983) found an increasing trend in the frequency of a rare kidney tumor in male mice.[28] The most recent study (1990) found an increase in pancreas and liver tumors in male rats together with an increase of the same thyroid cancer found in the 1983 study in females.[29]

There are no publicly available laboratory studies of the carcinogenicity of Roundup or other glyphosate-containing products.

All of these increases in tumor or cancer incidence are "not considered compound-related"[29] according to EPA (This means that EPA did not consider glyphosate the cause of the tumors.) For the testicular tumors, EPA accepted the interpretation of an industry pathologist who said that the incidence in treated groups (12%) was similar to those observed (4.5%) in other rats *not* fed glyphosate.[29] For thyroid cancer, EPA stated that it was not possible to distinguish between cancers and tumors of this type, so that the two should be considered together. The combined data are not statistically significant.[27] For kidney tumors, the manufacturer reexamined the tissue and found an additional tumor in untreated mice so that statistical significance was lost. This was despite the opinion of EPA's pathologist that the lesion in question was not really a tumor.[28] For pancreatic tumors, EPA stated that there was no dose-related trend. For liver and thyroid tumors, EPA stated that pairwise comparisons between treated and untreated animals were not statistically significant.[29]
EPA concluded that glyphosate should be classified as Group E, "evidence of non-carcinogenicity for humans."[29] They added that this classification "should not be interpreted as a definitive conclusion."[29] The cancer tests leave many questions unanswered. Concerning one of the carcinogenicity studies, an EPA statistician wrote, "Viewpoint is a key issue. Our viewpoint is one of protecting the public health when we see suspicious data."[30] Unfortunately, EPA has not taken that viewpoint in its assessment of glyphosate's cancer-causing potential. There are no publicly available laboratory studies of the carcinogenicity of Roundup or other glyphosate-containing products.

Mutagenicity

Although glyphosate's manufacturer describes "a large battery of assays"[31] showing that glyphosate does not cause genetic damage,[31] other studies have shown that both glyphosate and glyphosate products are mutagenic. Glyphosate-containing products are more potent mutagens than glyphosate.[32] The studies include the following:

- In fruit flies, Roundup and Pondmaster (an aquatic herbicide consisting of glyphosate and a trade secret surfactant[33]) both increased frequency of sex-linked, recessive lethal mutations. (These mutations are usually visible only in males.) Only a single concentration was tested in this study.[34]
- A study of human lymphocytes (a type of white blood cell) showed an increase in frequency of sister chromatid exchanges following exposure to the lowest dose tested of Roundup.[35] (Sister chromatid exchanges are exchanges of genetic material during cell division between members of a chromosome pair. They result from point mutations.) A 1997 study of human lymphocytes found similar results with Roundup (at both doses tested) and with glyphosate (at all but the lowest dose tested).[32]
- In *Salmonella* bacteria, Roundup was weakly mutagenic at two concentrations. In onion root cells, Roundup caused an increase in chromosome aberrations, also at two concentrations.[36]
- In mice injected with Roundup, the frequency of DNA adducts (the binding to genetic material of reactive molecules that lead to mutations) in the liver and kidney increased at all three doses tested.[37]
- In another study of mice injected with glyphosate and Roundup, frequency of chromosome damage and DNA damage increased in bone marrow, liver, and kidney. (Only a single concentration was tested in this study.)[32]

Reproductive effects

Glyphosate exposure has been linked to reproductive problems in humans. A study in Ontario, Canada, found that fathers' use of glyphosate was associated with an increase in miscarriages and premature births in farm families.[38] In addition, a case report from the University of California discussed a student athlete who suffered abnormally frequent menstruation when she competed at tracks where glyphosate had been used.[39]

Laboratory studies have also demonstrated a number of effects of glyphosate on reproduction. In rats, glyphosate reduced sperm counts at the two highest doses tested. In male rabbits, glyphosate at doses of 1/10 and 1/100 of the LD_{50} increased the frequency of abnormal and dead sperm.[40] In a study of female

rabbits, glyphosate caused a decrease in fetal weight in all treated groups.[41]

Human exposure

People are exposed to glyphosate through workplace exposure (for people who use glyphosate products on the job), eating of contaminated food, exposure caused by off-target movement following application, contact with contaminated soil, and drinking or bathing in contaminated water. The next sections summarize information about some of these routes of exposure.

Contamination of food: Analysis of glyphosate residues is "in general laborious, complex, and costly."[2] For this reason, it is not included in government monitoring of pesticide residues in food.[2] The only information available about contamination of food comes from research studies.

Monsanto's studies of residues in food crops found glyphosate in lettuce over five months after treatment (the lettuce was planted four months after treatment). Monsanto also found glyphosate in barley over four months after treatment (the barley was planted one month after treatment).[41a]

"Significant residues,"[2] according to the World Health Organization, have been identified from pre-harvest use of glyphosate on wheat (to dry out the grain). Bran contains between two and four times the amount on whole grains, and residues are not lost during baking.[2]

Occupational exposure: In California, the state with the most comprehensive program for reporting of pesticide-caused illness, glyphosate-containing herbicides were the third most commonly-reported cause of pesticide illness among agricultural workers.[42] Among landscape maintenance workers, glyphosate herbicides were the most commonly reported cause.[43] (Both these statistics come from illness reports collected between 1984 and 1990.) Even when glyphosate's extensive use in California is considered, and illness statistics presented as "number of acute illnesses reported per million pounds used in California," glyphosate ranked twelfth.[42]

While many of the California reports involve "irritant effects,"[44] mostly to eyes and skin, NCAP's survey of about 100 reports made in 1993, 1994, and 1995 found that over half of them involved more serious effects: burning of eyes or skin, blurred vision, peeling of skin, nausea, headache, vomiting, diarrhea, chest pain, dizziness, numbness, burning of the genitals, and wheezing.[45]

Persistence and movement in soil

Glyphosate's persistence in soil varies widely, so giving a simple answer to the question "How long does glyphosate persist in soil?" is not possible. Half-lives (the time required for half of the amount of glyphosate applied to break down or move away) as low as three days (in Texas) and as long as 141 days (in Iowa) have been measured by glyphosate's manufacturer.[46] Initial degradation (breakdown) is faster than the subsequent degradation of what remains.[47] Long persistence has been measured in the following studies: 55 days on an Oregon Coast Range forestry site[48]; 249 days on Finnish agricultural soils[49]; between 259 and 296 days on eight Finnish forestry sites[47]; 335 days on an Ontario (Canada) forestry site[50]; 360 days on three British Columbia forestry sites[51]; and, from one to three years on 11 Swedish forestry sites.[52] EPA's Ecological Effect's Branch wrote, "In summary, this herbicide is extremely persistent under typical application conditions."[53]

Glyphosate is thought to be "tightly complexed [bound] by most soils"[54] and therefore "in most soils, glyphosate is essentially immobile."[54] This means that glyphosate will be unlikely to contaminate water or soil away from the application site. However, this binding to soil is "reversible." For example, one study found that glyphosate bound readily to four different soils. However, desorption, when glyphosate unbinds from soil particles, also occurred readily. In one soil, 80% of the added glyphosate desorbed in a two hour period. The study concluded that "this herbicide can be extensively mobile in the soil...."[55]

Water contamination

When glyphosate binds readily to soil particles, it does not have the chemical characteristics of a pesticide that is likely to leach into water.[2] (When it readily desorbs, as described above, this changes.) However, glyphosate can move into surface water when the soil particles to which it is bound are washed into streams or rivers.[4] How often this happens is not known, because routine monitoring for glyphosate in water is infrequent.[2]

Glyphosate has been found in both ground and surface water. Examples include farm ponds in Ontario, Canada, contaminated by runoff from an agricultural treatment and a spill[56]; runoff from watersheds treated with Roundup during production of no-till corn and fescue[57]; contaminated surface water in the Netherlands[2]; seven U.S. wells (one in Texas, six in Virginia) contaminated with glyphosate[58]; contaminated forest streams in Oregon and Washington[59,60]; contaminated streams near Puget Sound, Washington[61]; and contaminated wells under electrical substations treated with glyphosate.[62]

Glyphosate's persistence in water is shorter than its persistence in soils. Two Canadian studies found glyphosate persisted 12 to 60 days in pond water.[63,64] Glyphosate persists longer in pond sediments (mud at the bottom of a pond). For example, the half-life in pond sediments in a Missouri study was 120 days; persistence was over a year in pond sediments in Michigan and Oregon.[4]

Effects on nontarget animals

Beneficial insects: Beneficial insects kill other species that are agricultural pests. The International Organization for Biological Control found that exposure to freshly dried Roundup killed over 50% of three species of beneficial insects: a parasitoid wasp, a lacewing, and a ladybug. Over 80% of a fourth species, a predatory beetle, were killed.[65]

Impacts on beneficial insects have also been shown in field studies, probably due to destruction of habitat by the herbicide. In North Carolina wheat fields, populations of large carabid beetles declined after treatment with a glyphosate product and did not recover for 28 days.[66] A study of Roundup treatment of hedgerows in the UK also showed a decline in carabid beetles.[67]

Other insects: Roundup treatment of a Maine clear-cut caused an 89% decline in the number of herbivorous (plant-eating) insects because of destruction of vegetation on which they live

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and feed. These insects serve as food resources for birds and insect-eating small mammals.[68] U.S. Fish and Wildlife Service has identified one endangered insect, a longhorn beetle, that would be jeopardized by use of glyphosate herbicides.[69]

Other arthropods: Glyphosate and glyphosate-containing products kill a variety of other arthropods. For example, over 50% of test populations of a beneficial predatory mite were killed by exposure to Roundup.[65] In another laboratory study, Roundup exposure caused a decrease in survival and a decrease in body weight of woodlice. These arthropods are important in humus production and soil aeration.[70] Roundup treatment of hedgerows reduced the number of spiders, probably by killing plants they preferred for web-spinning.[67] The water flea *Daphnia pulex* is killed by concentrations of Roundup between 3 and 25 ppm.[71-73] Young *Daphnia* are more susceptible than mature individuals.[72] The red swamp crawfish, a commercial species, was killed by 47 ppm of Roundup.[74]

Both glyphosate and commercial products that contain glyphosate are acutely toxic to fish.

Earthworms: A study of the most common earthworm found in agricultural soils in New Zealand showed that repeated applications of glyphosate significantly affect growth and survival of earthworms. Biweekly applications of low rates of glyphosate (1/20 of typical rates) caused a reduction in growth, an increase in time to maturity, and an increase in mortality.[75]

Fish: Both glyphosate and commercial products that contain glyphosate are acutely toxic to fish. In general, glyphosate alone is less toxic than the common glyphosate product, Roundup, and other glyphosate products have intermediate toxicity. Part of these differences can be explained by toxicity of the surfactant (detergent-like ingredient) in Roundup. It is 20 to 70 times more toxic to fish than glyphosate itself.[71]

Acute toxicities of glyphosate vary widely: median lethal concentrations (LC_{50}s; the concentrations killing 50% of a population of test animals) from 10 ppm to over 200 ppm have been reported depending on species of fish and test conditions.[2] Acute toxicities (LC_{50}) of Roundup to fish range from 2 ppm to 55 ppm.[2] Part of this variability is due to age: young fish are more sensitive to Roundup than older fish.[71] Acute toxicities of Rodeo (used with the surfactant X-77 per label recommendations) vary from 120 to 290 ppm.[76]

In soft water there is little difference between toxicities of glyphosate and Roundup.[77] Also, if fish have not recently eaten, the toxicity of glyphosate (LC_{50} = 2.9 ppm) is similar to that of Roundup.[78]

Roundup toxicity increases with increased water temperature. In both rainbow trout and bluegills, toxicity about doubled between 7 and 17°C (45 and 63°F).[71] Treatment of riparian areas with glyphosate causes water temperatures to increase for several years following treatment[79] because the herbicide kills shading vegetation. This means that use of glyphosate could cause increased toxicity to fish. In addition, temperature increase could be critical for fish, like juvenile salmon, that thrive in cold water.

Sublethal effects of glyphosate occur at low concentrations. In rainbow trout and *Tilapia* concentrations of about 1/2 and 1/5 of the LC_{50} (respectively) caused erratic swimming.[80,81] Trout also exhibited labored breathing.[80] These effects can increase the risk that fish will be eaten, as well as affecting feeding, migration, and reproduction.[81] Less than 1% of the LC_{50} caused gill damage in carp and less than 2% caused changes in liver structure.[82]

Birds: Glyphosate has indirect impacts on birds. Because glyphosate kills plants, its use can create a dramatic change in the structure of the plant community. This affects bird populations, since birds depend on plants for food, shelter, and nest support.

For example, a study of four glyphosate-treated clear-cuts (and an unsprayed control plot) in Nova Scotia found that densities of the two most common species of birds (white-throated sparrow and common yellowthroat) decreased for two years after treatment. By the fourth year post-spray, densities had returned to normal for these two species. By then the unsprayed plot had been colonized by new species of birds (warblers, vireos, and a hummingbird) which were not found on sprayed plots.[83]

An earlier three year study of songbird abundance following glyphosate treatment of clear-cuts in Maine forests showed similar results. Abundances of total number of birds and three common species decreased. Decrease in bird abundance was correlated with decrease in diversity of habitat.[84]

Black grouse avoided glyphosate-treated clear-cuts in Norway for several years after treatment.[85] Researchers recommended that the herbicide not be used near grouse courtship areas.

Small mammals: In field studies, small mammals have been indirectly affected when glyphosate kills the vegetation they (or their prey) use for food or shelter. On clear-cuts in Maine,[68] insect-eating shrews declined for three years post-treatment; plant-eating voles declined for two. A second study in Maine after a Roundup treatment[86] found similar results for voles. In British Columbia, deer mice populations were 83% lower following glyphosate treatment.[87] Another study from British Columbia found declines in chipmunk populations after Roundup treatment.[88] In Norway, there was a "strong reduction" in use of sprayed clear-cuts by mountain hare.[89] Other studies have not found impacts on small mammals,[90] suggesting that the particular characteristics of the site and the herbicide application are significant.

Wildlife: Canadian research has documented that plants serving as important food sources for wildlife are significantly damaged by glyphosate. "Severe" or "very severe damage" was recorded for 46% of important food species eaten by moose, between 34 and 40% of species eaten by elk, and 36% of species eaten by mule deer.[91]

Effects on nontarget Plants

Endangered species: Because many plants are susceptible to glyphosate, it can seriously impact endangered plant species. U.S. Fish and Wildlife Service has identified 74 endangered plant species that it believes could be jeopardized by glyphosate. This list is based on use of glyphosate on nine crops, and does not include over 50 other uses.[69]

Seed Quality: Sublethal treatment of cotton with Roundup "severely affects seed germination, vigor and stand establishment under field conditions." At the lowest glyphosate rate tested, seed germination was reduced between 24% and 85% and seedling weight was reduced between 19% and 83%.[92]

Nitrogen fixation: Most living things cannot use nitrogen in its common form and instead use ammonia and nitrates, much rarer compounds created by processes called nitrogen fixation and nitrification. They are carried out by bacteria which can be found in soil and in nodules on roots of legumes and certain other plants.[93]

Studies showing effects of glyphosate on nitrogen fixation include the following: At a concentration corresponding to typical application rates, glyphosate reduced by 70% the number of nitrogen-fixing nodules on clover planted 120 days after treatment[94]; a similar concentration of a glyphosate herbicide reduced by 27% the number of nodules on hydroponically grown clover[95]; a similar concentration of glyphosate reduced by 20% nitrogen-fixation by a soil bacteria[96]; a concentration of glyphosate approximately that expected in soybean roots following treatment inhibited the growth of soybean's nitrogen-fixing bacteria between 10% and 40%[97]; and treatment with a glyphosate herbicide at the lowest concentration tested (10 times typical application rates) reduced the number of nodules on clover between 68 and 95%.[98]

The studies summarized above were done in the laboratory. In the field, such effects have been difficult to observe. However, use of genetically-engineered glyphosate-tolerant crop plants means that nitrogen-fixing bacteria in field situations "could be affected by repeated applications of glyphosate."[97]

Glyphosate also impacts other parts of the nitrogen cycle. A Canadian study found that treatment of a grass field with Roundup increased nitrate loss up to seven weeks after treatment. The increase was probably caused by nutrients released into the soil by dying vegetation.[99]

Mycorrhizal fungi: Mycorrhizal fungi are beneficial fungi that live in and around plant roots and that help plants absorb nutrients and water and can protect them from cold and drought.[100] Roundup is toxic to mycorrhizal fungi in laboratory studies. Effects on some species associated with conifers have been observed at concentrations of one part per million (ppm), lower than those found in soil following typical applications.[101,102] In orchids, treatment with glyphosate changed the mutually beneficial interaction between the orchid and its mycorrhizae into a parasitic interaction (one that does not benefit the plant).[103]

Plant diseases: Glyphosate treatment increases susceptibility of crop plants to a number of diseases. For example, glyphosate increased susceptibility of tomatoes to crown and root disease[104]; reduced the ability of bean plants to defend themselves against the disease anthracnose[105]; increased growth of take-all disease in soil from a wheat field and decreased the proportion of soil fungi which was antagonistic to take-all fungus[106]; and increased soil populations of two important root pathogens of peas.[107] In addition, Roundup injection of lodgepole pine inhibited the defensive response of the tree to blue stain fungus.[108]

Both inhibition of mycorrhizae and increased susceptibility to disease have been observed in laboratory, not field, studies. Given the serious consequences these kinds of effects could have, more research is crucial.

Plant resistance

Plants that are resistant to glyphosate are able to tolerate treatment without showing signs of toxicity. Although many weed scientists argue that "it is nearly impossible for glyphosate resistance to evolve in weeds,"[109] others argue that "there are few constraints to weeds evolving resistance." The second group of scientists appears to be correct. In 1996 an Australian researcher reported that a population of annual ryegrass had developed resistance and tolerated five times the recommended field application rate.[110]

Source: Pages 38-43 of this publication are drawn from Global Pesticide Campaigner, April 1999, Vol. 9, No. 1. Published by Pesticide Action Network-NA, San Francisco, USA

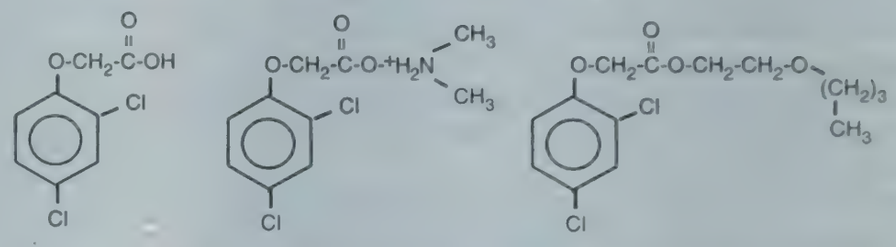
2,4-D: Toxicology

A factsheet by the Northwest Coalition for Alternatives to Pesticides (NCAP).

- **2,4-D is the most widely used herbicide in the world. Almost 60 million pounds are used annually in the U.S. including an estimated 35 million lawn and garden applications.**
- **Symptoms of 2,4-D poisoning include drowsiness, vomiting, convulsions, kidney and liver injury, and muscle twitching. 2,4-D and its salts that are used in herbicide products are severe eye irritants. Three of these salts cause skin lesions.**
- **2,4-D is unusual among herbicides in that it causes an array of adverse effects to the nervous system. 2,4-D has also caused genetic damage in tests using both cell cultures and laboratory animals.**
- **Studies of male farmers exposed to 2,4-D have found that exposed farmers have low-quality sperm. In addition, farmer-applicators in areas of high 2,4-D use have more children with birth defects than unexposed men.**
- **2,4-D exposure has been linked with increased risk of the cancer non-Hodgkin's lymphoma in a series of studies. 2,4-D has also been found to disrupt the normal functions of hormone systems.**
- **The U.S. Environmental Protection Agency has reported that 2,4-D is contaminated with dioxins, including the notorious 2,3,7,8-TCDD. TCDD causes a variety of reproductive problems, cancer, and damage to the immune system.**

By Caroline Cox

2,4-D and Some of Its Salts and Esters



2,4-D | dimethylamine salt of 2,4-D | butoxyethyl ester of 2,4-D

The herbicide 2,4-D (2,4-dichlorophenoxyacetic acid) is a widely used member of the phenoxy family.[1] It is currently manufactured by AGRO-GOR, Dow AgroSciences, and Nufarm, U.S.A[2] and is sold under a immense variety of brand names, including many "weed & feed" home use products.[3] It is a selective herbicide with highest toxicity to broadleaf plants.[1] The acid form is occasionally used in commercial herbicide products; three salts (the dimethylamine, triisopropanolamine, and isopropylamine) and two esters (the isooctyl ester and the butoxyethyl ester) are commonly used.[4]

2,4-D was first registered for use in the U.S. in 1948,[5] and is now undergoing the reregistration process in which health and safety testing for older pesticides is brought up to current standards.[6]

Use

2,4-D is "the most widely used herbicide in the world," according to a consortium of 2,4-D manufacturers.[2] The U.S. Environmental Protection Agency (EPA) estimates that U.S. use is 58 million pounds per year, with lawn and garden uses accounting for nine million pounds; industrial, commercial and government uses accounting for 13 million; and agriculture accounting for 36 million.[7]

U.S. households make an estimated 35 million applications of 2,4-D annually.[8]

The U.S. Department of Agriculture surveyed agricultural 2,4-D use patterns in 1996 and found that major uses included control of unwanted plants in pasture, fallow land, rangeland, wheat, corn and turf.[9]

"Inert" Ingredients

Like most pesticide products, many commercial 2,4-D products contain "inerts," ingredients added to make pesticides more potent or easier to use whose identity is often not publicly available. Where available, information about the toxicology of commercial 2,4-D products, including "inerts," is included in the following discussion. Specific information about the toxicology of "inerts" used in 2,4-D products will be summarized in the next part of this factsheet.

Acute toxicity

According to the National Toxicology Program, symptoms of short-term exposure to 2,4-D include drowsiness, nausea, vomiting, convulsions, coma, kidney and liver injury, hepati-

Source: Pesticide Action Network-NA, San Francisco, USA

tis, diarrhea, weakness, muscle twitching, loss of reflexes, headache, numbness or pain in the arms and legs, sweating and incontinence.[10]

Case reports published by physicians provide more detailed accounts. One patient spilled about 1/4 cup (60 milliliters) of a 10% solution of a 2,4-D ester on his forearms. That evening he felt fatigued, and for ten days suffered from nausea, vomiting, and a 20 pound weight loss. A second patient accidentally sprayed a 2,4-D ester solution on his sleeves and pant legs, and inhaled the spray. The following day he had a headache, and vomited.[11]

Eye irritation

2,4-D and its dimethylamine, diethanolamine, isopropylamine, and triisopropanolamine salts are "severe eye irritants" which cause eye lesions lasting at least three days. In long-term feeding studies at relatively high doses, 2,4-D has also caused degeneration of the retina and cataracts.[12]

For information about the eye irritation caused by commercial 2,4-D products, NCAP surveyed material safety data sheets (MSDSs) and labels for 56 products. Of the products surveyed, 50 warned of eye irritation hazards. Over 20 of these were "corrosive" or caused "substantial" or "irreversible" eye damage. The others warned of moderate damage.[4]

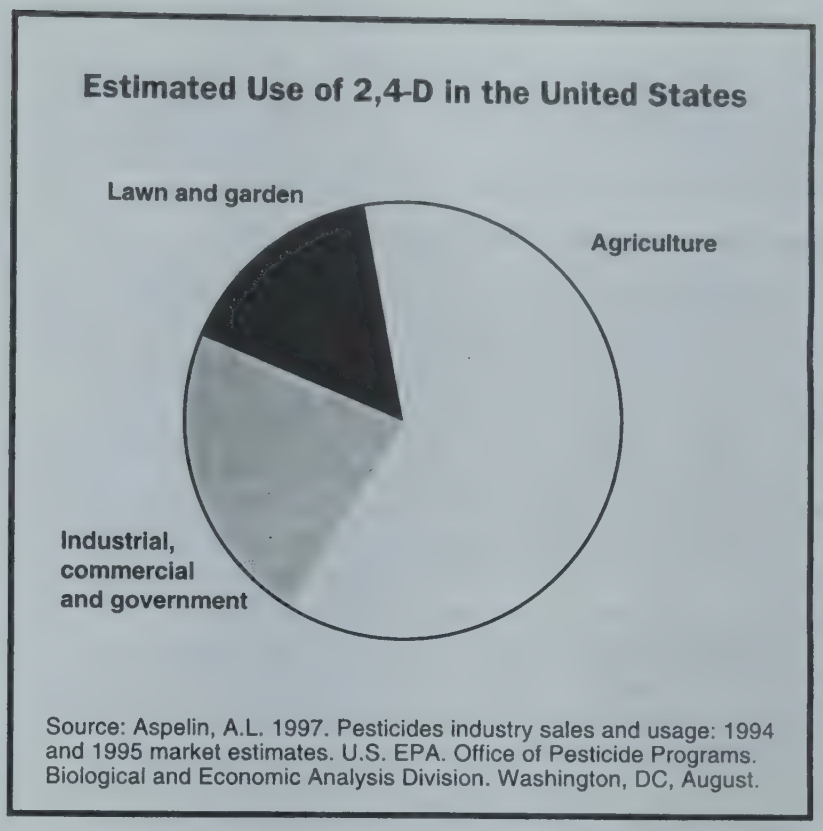
Skin irritation

In rabbits, 2,4-D is "mildly irritating" to the skin. Three 2,4-D salts (dimethylamine, diethanolamine, and isopropylamine) cause skin lesions.[12] In NCAP's survey of MSDSs and labels of commercial 2,4-D products, we found that half of them contained warnings of skin irritation, including skin sensitization or the development of allergic reactions in susceptible people.[4]

Neurotoxicity

Although many common insecticides target the nervous system, 2,4-D is unusual among herbicides because it has an array of adverse effects on the nervous system. One of the most common neurotoxic symptoms associated with 2,4-D exposure is myotonia. Myotonia occurs when muscles are unable to relax after a voluntary contraction.[13] Myotonia is routinely induced in laboratory experiments by administering 2,4-D.[13-15]

2,4-D has also caused peripheral neuropathy, a condition involving unusual sensations, numbness, and pain in the arms and legs, as well as incoordination and unsteadiness when walking.[16] This disability can be protracted, and recovery incomplete. Examples of cases reported by physicians include a farmer who lost the ability to walk six weeks after spilling 2,4-D on his clothing. A year later the patient was still using crutches to walk, and two years later had not regained movement of his toes. A homeowner developed peripheral neuropathy after kneeling on her 2,4-D-treated lawn. She lost 20 pounds and was unable to walk for a period of weeks. Three years later she was still "clumsy on her feet," according to her physician, and was only two thirds recovered.[17] Another farmer lost hand control after spraying 2,4-D on his cornfield; a year later he still complained of intermittent numbness.[17] Individuals seem to vary considerably in how susceptible they are to neuropathy caused by 2,4-D.[17]



Source: Aspelin, A.L. 1997. Pesticides industry sales and usage: 1994 and 1995 market estimates. U.S. EPA. Office of Pesticide Programs. Biological and Economic Analysis Division. Washington, DC, August.

In experiments with laboratory animals, 2,4-D affects behavior. In rats, single oral doses of 2,4-D decreased how much they walked, decreased the number of times they reared on their hind legs, and increased the amount of time they were still. These behavioral effects were associated with changes in the levels of serotonin and its breakdown product in the brain.[18] Serotonin is one of the chemicals used in the brain to transmit nerve impulses from one nerve cell to another. Another experiment showed that 2,4-D reduced the frequency of learned behaviors in rats.[19] Similar behavioral effects have been caused by 2,4-D butoxyethyl ester: a reduced amount of walking and an increase in incoordination.[20,21] The incoordination is probably caused by n-butanol, a breakdown product of the butoxyethyl ester, but the effects on movement appear to be caused by 2,4-D itself.[21]

Laboratory experiments also indicate that children's nervous systems might be especially affected by 2,4-D exposure. In rats, exposure of growing juvenile rats (during the first 2-3 weeks after birth) reduced the size of the brain and altered components of the membranes in nerve cells.[22] When juvenile rats are exposed to 2,4-D through their mother's milk, they develop less myelin (a covering on nerve cells) than normal.[23] Exposure of juvenile rats to the butoxyethyl ester of 2,4-D resulted in reduced brain weight, changes in the levels of neurotransmitters, and impaired learning ability.[24] When juvenile rats were exposed both during pregnancy and nursing, levels of serotonin in the brain permanently increased.[25]

These studies showing how 2,4-D affects the nervous system are supported by studies showing that 2,4-D travels to

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the brain after animals are dosed with the herbicide. At high doses, 2,4-D damages the blood-brain barrier, allowing 2,4-D to penetrate brain tissue,[26] but 2,4-D also reaches the brain at doses as low as 1/100 of the acute lethal dose.[27]

Effects on the circulatory system

2,4-D disrupts the ability of the blood to carry oxygen, and also inhibits the blood clotting process.

Scanning electron micrographs of human red blood cells show that 2,4-D has a dramatic effect on the shape of red blood cells (cells that carry oxygen). This effect is caused by 2,4-D's ability to perturb red blood cell membranes.[28] 2,4-D also decreases the affinity that hemoglobin has for oxygen.[29]

In human blood, platelet aggregation (the process of blood clotting) is inhibited by 2,4-D.[30, 31] Inhibition of clotting also occurs in rabbit blood following injection of 2,4-D.[30]

There are no publicly available laboratory studies of the effect of commercial 2,4-D products on the circulatory system. However, NCAP's survey of label and MSDSs for 56 2,4-D products found that seven of them warn that exposure can cause a decrease in blood pressure.[4]

Subchronic toxicity

In medium-term (subchronic) toxicity tests using rats, EPA found the most significant adverse effects were found in the blood and kidneys.[32] After seven weeks, hemoglobin (oxygen-carrying protein) levels in the blood decreased, as did the number of red blood cells, consistent with the studies summarized in the previous section. The decrease was statistically significant at all but the lowest dose tested (1 milligram per kilogram (mg/kg) of body weight per day). EPA set 2,4-D's reference dose, the "daily exposure that is likely to be without an appreciable risk of deleterious effects during a lifetime," based on this study,[32] although 2,4-D manufacturers support a 15-fold increase.[1] In addition, at all but the two lowest doses tested in this study, kidney weights increased and pathology of the kidney was observed.

Other medium-term studies have found 2,4-D caused loss of muscle and body weight, or decreased weight gain.[33-35]

Chronic toxicity

Chronic (long-term) feeding studies with laboratory animals show effects similar to those found in the subchronic studies. In a two-year study with rats, 2,4-D caused kidney lesions at all but the lowest dose tested (1 mg/kg of body weight). In a one-year study with dogs, 2,4-D caused a decrease in weight gain and lesions in the liver and kidney, again at all doses except the lowest. The World Health Organization used these results to set its "acceptable daily intake."[12]

Chronic effects of 2,4-D have also been reported in people. Several physicians have published reports of liver disease (hepatitis) associated with exposure to 2,4-D. In both cases the patients were golfers who habitually licked their golf balls while playing on 2,4-D-treated golf courses.[36-37]

There are no publicly available chronic or subchronic laboratory studies of commercial 2,4-D products (containing 2,4-D and "inert" ingredients)

Mutagenicity

A study of herbicide applicators spraying 2,4-D found that white blood cells with multiple nuclei (chromosome-containing structures) were more common in applicators at the end of the spraying season than before the season began. Applicators also had more multiple nuclei than workers not exposed to 2,4-D.[38]

Although government evaluations of laboratory studies of 2,4-D have concluded that it does not cause genetic damage,[14, 39] in fact it has been mutagenic in a variety of studies. These include both studies using live animals and studies using cell cultures.

Animals: When administered in rabbits' drinking water, the sodium salt of 2,4-D caused an increase in the number of brain cells with unusual numbers of chromosomes or cells with multiple chromosome sets.[40] Dermally applied 2,4-D caused an increase in the number of abnormalities in the nuclei of hair follicle cells in mice.[41] 2,4-D also increased the frequency of abnormal chromosomes in the bone marrow cells of mice[42] and rats[43] fed 2,4-D.

Human cell cultures: The dimethylamine salt of 2,4-D caused breaks in DNA molecules (genetic material) from human connective tissue.[44] Commercial products containing the amine salt of 2,4-D,[45] and 2,4-D acid,[42] caused chromosome aberrations in cultured human white blood cells. Also in white blood cells, 2,4-D acid caused an increase in sister chromatid exchanges,[46] the exchange of DNA between parts of a duplicating chromosome.[47]

Other cell cultures: When cultured cells from hamster connective tissue were exposed to 2,4-D, the frequency of mutations at a particular gene, called the HGPRT locus, increased.[48] In cultures of cow muscle cells, 2,4-D increased the frequency of polyploid cells (those with multiple sets of chromosomes) as well as cells with other chromosome abnormalities.[49]

Simultaneous exposure to several chemicals may increase the genetic damage caused by 2,4-D. In cultures of human connective tissue cells, copper and 2,4-D together caused DNA damage and repair that was not caused by either chemical alone.[50]

Effects on reproduction

Evidence that exposure to 2,4-D can adversely affect reproductive function comes from studies of male farmers. In one study, exposed farmers had lower quality of sperm than did unexposed farmers. Exposed farmers' sperm counts were 52% lower, the frequency of abnormal sperm was doubled, and the ability of the sperm to move was reduced compared to sperm from unexposed farmers. Exposure was verified by urine analysis: exposed farmers' urine contained an average of nine parts per million (ppm) of 2,4-D while none was found in urine from unexposed farmers.[51]

A 1996 study of private pesticide appliers (farmers licensed to apply restricted-use pesticides on their farms) in Minnesota

also associated 2,4-D use with adverse effects on reproduction. The study found that the birth defect rate was higher in children of private appliers than in the general population, and that the birth defect rate for children of appliers was highest in western Minnesota where use of phenoxy herbicides (primarily 2,4-D and MCPA) was highest. The birth defect rate was highest for children of western Minnesota appliers conceived in the spring, when phenoxy herbicides are applied. Finally, corroborating the sperm quality study, the frequency of births among pesticide appliers in high phenoxy herbicide use counties was about half that of the general population in those counties.[52]

Laboratory studies of 2,4-D's effects on reproduction in rats have shown that relatively high doses of 2,4-D cause extra ribs, misalignment and slow bone formation in the backbone, and other rib abnormalities.[53, 54]

Concerns about 2,4-D's effects on reproduction are increased by laboratory studies showing that 2,4-D is found in the brain and blood of fetuses after dosing of mother animals.[55, 56] Repeated exposures increase accumulation of 2,4-D.[57]

There are no publicly available laboratory studies of commercial 2,4-D products' effects on reproduction. However, NCAP's survey of 56 2,4-D products found that four have warnings about damage to the testes.[58]

Gender differences in susceptibility to 2,4-D

Laboratory tests have shown that there are complex gender differences in the way 2,4-D affects animal physiology. In rats, females are not able to rid the body of 2,4-D as quickly as are males, leading to higher concentrations of 2,4-D in females. In hamsters, the reverse is true.[59] In rats, effects of 2,4-D butyl ester on behavior (the ability to balance on a spinning rod) were observed in males and pregnant females, but not in nonpregnant females. A similar pattern was observed with respect to learning an avoidance behavior.[60]

Carcinogenicity

2,4-D's ability to cause cancer has been controversial since the 1970s when a Swedish oncologist reported that many of his lymphoma patients had been exposed to phenoxy herbicides (including 2,4-D) and the related chlorophenols.[61] Since that time the association between 2,4-D exposure and cancer has been frequently studied. Epidemiologists (scientists who study the causes of disease in actual patients rather than laboratory animals) have focused on non-Hodgkin's lymphoma (NHL), the sixth most common cancer in the U.S. and one whose incidence is increasing.[62]

Studies which have found an association between 2,4-D exposure and NHL include the following:

- The National Cancer Institute (NCI) studied the incidence of NHL among Kansas men, and found that men with NHL were more likely to have used farm herbicides than men without the disease. Looking at just 2,4-D exposure, men with NHL were 2.6 times more likely to have used 2,4-D than men without the disease. The relative risk of NHL increased with the number of days of herbicide exposure per year and the length of time since the first exposure. Frequent herbicide users had a six-fold increase in risk.[63]
- A second study by NCI[64] conducted in Nebraska found a similar association between use of 2,4-D and NHL. Overall, the study found "a 50% excess of NHL associated with mixing or applying 2,4-D."[64] As in the Kansas study, risk increased with increasing number of days that 2,4-D was used.

This study, and the Kansas study, were criticized because they obtained information about herbicide exposure from spouses if the farmers themselves had died. NCI then did two studies to compare responses from farmers and spouses and found that agreement was excellent on yes/no questions and adequate on more detailed questions.[65] While the reliability of responses about pesticide use are "lower than desired," the biases this introduces would tend to obscure any association between disease and pesticide use, and thus strengthens the results of the Kansas and Nebraska studies.[66]

- A study by the Laboratory Centre for Disease Control (Canada) found that the risk of NHL in male Saskatchewan farmers increased with the acreage they sprayed with herbicides. Herbicide use by Saskatchewan farmers during the years of the study was 75%-90% 2,4-D.[67]
- A third National Cancer Institute study found that dogs with canine malignant lymphoma (the canine equivalent of NHL) were more likely than healthy dogs to live in households where owners applied 2,4-D to their lawn or employed lawn care companies to treat their yard for weeds. Risks were highest when both commercial and owner applications were made and in households making four or more applications per year.[68] A task force of 2,4-D manufacturers sponsored a detailed critique of the study,[69] but most of these have been answered by the study's authors.[70] A follow-up study showed that dogs living in homes with 2,4-D treated lawns had high urinary 2,4-D levels.[71]
- A study of workers in a U.S. 2,4-D manufacturing plant found that cancers of the lymph system were three times more frequent than expected.[72] The incidence of NHL remained high in a follow-up study.[73] In four British factories manufacturing phenoxy herbicides, the incidence of non-Hodgkin's lymphoma was two times higher than expected.[74]
- Among employees of the lawn care company ChemLawn, the incidence of NHL for male lawn applicators was about 1.6 times that expected. The incidence among applicators employed over three years was seven times that expected. More follow-up is planned.[75] A study of golf course superintendents, who often apply herbicides, found that the death rate from non-Hodgkin's lymphoma were approximately double the expected rate.[76]
- Studies of smaller populations have also found an association between 2,4-D use and NHL. In a rural, agriculturally based community in New York where 2,4-D was "widely used" the incidence of NHL was 1.5 times higher than expected.[77] In northern Italy, the incidence of NHL was increased in areas where phenoxy herbicides had been detected in soil or water and increased markedly in areas with the highest contamination levels.[78] Around Milan, Italy, people with NHL were more likely to have been occupationally

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exposed to herbicides than people without the disease, and researchers found a significant trend with duration of exposure.[79] Among Danish gardeners, the incidence of NHL was twice the expected rate.[80] Agriculture and forestry workers from three Swedish counties who were exposed to phenoxy herbicides were four times more likely to develop malignant lymphomas than unexposed workers.[81]

Nine other epidemiological studies have either failed to find a relationship between 2,4-D and NHL, or have found a relationship that was weaker than those summarized above.[82]

Carcinogenicity studies of laboratory animals submitted in support of 2,4-D's registration have not demonstrated increased risks of lymphoma.[82] However, a study conducted by the Food and Drug Administration in 1971 found that the incidence of lymphoma in rats exposed to 2,4-D was 4%, while no lymphoma occurred in unexposed rats.[83]

There are no publicly available laboratory studies of the carcinogenicity of commercial 2,4-D products.

The scientists who conducted the NCI studies stated that they "believe that the weight of evidence indicates that the use of 2,4-D in an agricultural setting increases the risk of NHL among persons handling the chemical frequently."[64] Yet, government evaluations of 2,4-D's carcinogenicity are less straightforward. 2,4-D is classified as "possibly carcinogenic to humans" (for phenoxy herbicides as a group) by the International Agency for Research on Cancer[84] and as "not classifiable as to human carcinogenicity" by the U.S. Environmental Protection Agency.[82]

2,4-D presents "a dilemma to the scientific community in how to draw conclusions regarding carcinogenicity when the epidemiologic and experimental data do not agree,"[85] wrote NCI epidemiologist Aaron Blair. "The challenge in the future will be to design studies in the laboratory that mimic the human condition."[85]

In the meantime, although conflicting data are inevitable when studying the complex association between disease and pesticide exposure, eliminating 2,4-D use will protect public health.

Recent research has shown that 2,4-D has biological activity similar to chemicals that stop the growth of human cancer cells and are being considered for use as anticancer drugs.[86] This research does not contradict the research showing that occupational exposure to 2,4-D increases the risk of NHL. Many drugs used to treat, or even prevent cancer, also cause cancer. Examples include tamoxifen, cisplatin, and melphalan.[87]

Endocrine disruption

Significant research and regulatory resources have been focused recently on chemicals that disrupt the normal functions of the endocrine system, the glands and hormones that regulate the growth and development of animals. Although much research remains to be done, experimental evidence suggests that 2,4-D disrupts animal endocrine systems.

Thyroxine is a hormone produced by the thyroid that is involved in the regulation of metabolism. In rats, 2,4-D "markedly increases" iodine uptake by the thyroid,[88] and decreases the ability of blood to bind with thyroxine.[89] In addition, 2,4-D changes the distribution of thyroxine in the body, so that more is stored in the liver and brain.[88] In sheep, a commercial 2,4-D product decreases blood concentrations of thyroxine.[90]

Leydig cells are testes cells that produce testosterone, often called the male sex hormone as well as estrogens, often called female sex hormones. Rat Leydig cells exposed to 2,4-D increase their production of estradiol, an estrogen.[91]

Effects on the immune system

A study of ten Italian farmers who used phenoxy herbicides (2,4-D and the related herbicide MCPA) found a variety of changes in the immune system. The study compared blood samples taken prior to herbicide use with samples taken just after herbicide use. The numbers of five kinds of T cells decreased. T cells are white blood cells with immunological activity. In addition, the numbers of natural killer cells and their activity decreased. Natural killer cells are "directly involved in cell mediated immunity to tumors." Finally, the response of the immune system to two foreign chemicals dropped sharply. Two months after exposure, some of the changes persisted.[92]

Contaminants

Dioxins are a family of compounds that include "extremely toxic and potent"[93] chemicals. Dioxins gained notoriety as contaminants of the 2,4-D-containing herbicide Agent Orange used during the Vietnam War.[93] The little testing that has been done shows that current 2,4-D products are contaminated with dioxins,[94] including 2,3,7,8-TCDD,[94] the most toxic dioxin.[93] 2,3,7,8-TCDD was found in two of the eight samples analyzed for EPA by 2,4-D manufacturers.[94] A closely related dioxin (1,2,3,7,8-pentachlorodibenzo-p-dioxin) was found in three of the eight samples tested.[94] The Washington Department of Agriculture recently surveyed fertilizer products, including one 2,4-D-containing product. Their analysis showed that it was contaminated with 2,3,7,8-TCDD and the same pentadioxin found by EPA as well as three related dioxins.[95]

Adverse health effects associated with 2,3,7,8-TCDD and other dioxins include wasting disease (weight loss), chloracne (a severe skin disease), an increased risk of diabetes, weakening of the immune system, decreased fertility, alterations in levels of sex hormones, increased risk of miscarriages, decreased sperm production, increased frequency of severe birth defects, and cancer. Dioxins are persistent and increase in concentration as they move up the food chain.[93]

Source: Pages 44-48 of this publication are drawn from Global Pesticide Campaigner, August 1999, Vol. 9, No. 2. Published by Pesticide Action Network-NA, San Francisco, USA

Permethrin

A factsheet by the Northwest Coalition for Alternatives to Pesticides (NCAP).

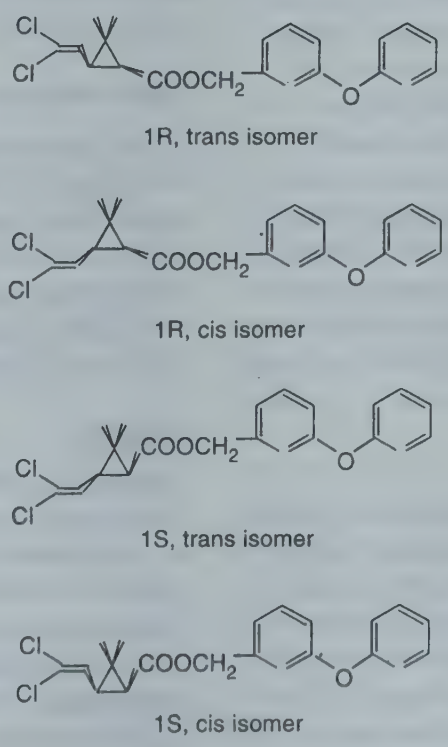
- **The insecticide permethrin (in the synthetic pyrethroid family) is widely used on cotton, wheat, corn, alfalfa, and other crops. In addition, over 100 million applications are made annually in and around U.S. homes.**
- **Permethrin, like all synthetic pyrethroids, is a neurotoxin. Symptoms include tremors, incoordination, elevated body temperature, increased aggressive behavior, and disruption of learning. Laboratory tests suggest that permethrin is more acutely toxic to children than to adults.**
- **The U.S. Environmental Protection Agency has classified permethrin as a carcinogen because it causes lung tumors in female mice and liver tumors in mice of both sexes. Permethrin inhibits the activity of the immune system in laboratory tests, and also binds to the receptors for a male sex hormone. It causes chromosome aberrations in human and hamster cells.**
- **Permethrin is toxic to honey bees and other beneficial insects, fish, aquatic insects, crayfish, and shrimp. For many species, concentrations of less than one part per billion are lethal. Permethrin causes deformities and other developmental problems in tadpoles, and reduces the number of oxygen-carrying cells in the blood of birds.**
- **Permethrin has been found in streams and rivers throughout the United States. It is also routinely found on produce, particularly spinach, tomatoes, celery, lettuce, and peaches.**
- **A wide variety of insects have developed resistance to permethrin. High levels of resistance have been documented in cockroaches, head lice, and tobacco budworm.**

by Caroline Cox

Permethrin is used to kill pest insects in agriculture, home pest control, forestry, and in public health programs, including head lice control. It was first marketed in 1973. Worldwide, the dominant use of permethrin is on cotton, accounting for about 60% (by weight) of the permethrin used.[1] In the U.S., almost 70% of the permethrin used in agriculture is used on corn, wheat, and alfalfa.[2] Over 100 million applications of permethrin are made each year in U.S. homes, and over 18 million applications are made in yards and gardens.[3]

Permethrin is a synthetic pyrethroid. Like most members of this family of insecticides, it has four isomers, molecules made up of the same atoms with different three-dimensional structures. 1R,cis-permethrin is the most insecticidally active isomer.[4]

Permethrin



1R, trans isomer

1R, cis isomer

1S, trans isomer

1S, cis isomer

3-Phenoxybenzyl-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropanecarboxylate

Mode of action

Permethrin, like all synthetic pyrethroids, kills insects by strongly exciting their nervous systems. Permethrin makes the nervous system hypersenstitive to stimuli from sense organs. Rather than sending a single impulse in response to a stimulus, permethrin-exposed nerves send a train of impulses. This excitation occurs because permethrin blocks the movement of sodium ions from outside to inside of the nerve cells. Permethrin's mode of action is similar to that of the organochlorine insecticide DDT.[5]

Acute lethal dose

Permethrin's LD_{50} (the amount of permethrin that kills 50% of a population of test animals) is variable. In a summary of nine oral LD_{50} tests using rats, the LD_{50} varied from 430 milligrams per kilogram of body weight (mg/kg) to over 4,000 mg/kg. Some of this variability occurs because the proportions of isomers in the test materials vary. The cis isomers are about ten times more toxic than the trans isomers.[6]

Neurotoxicity

In mammals, permethrin has complex effects on the nervous system. As in insects, it causes repetitive nerve impulses. It also inhibits a variety of nervous system enzymes: ATPase, whose inhibition results in increased release of the neurotransmitter acetylcholine[7]; monoamine oxidase-A, the enzyme which maintains normal levels of three other neurotransmitters[8]; and acetylcholinesterase, the enzyme that breaks down acetylcholine.[9] (Two large families of insecticides, the organophosphates and the carbamates, are acetylcholinesterase inhibitors.) In addition, permethrin inhibits a nervous system receptor, the $GABA_A$ receptor, producing excitability and convulsions.[10] Finally, permethrin inhibits

Source: Pesticide Action Network-NA, San Francisco, USA

respiration (the process by which cells use sugars as an energy source) in a manner similar to other neurotoxic drugs.[11] It is therefore not surprising that permethrin causes a wide variety of neurotoxic symptoms.

At relatively high doses, these neurotoxic symptoms of permethrin include tremors, incoordination, hyperactivity, paralysis, and an increase in body temperature. These symptoms can persist up to three days.[12] Other behavioral effects have been observed at lower doses. For example, sublethal exposure of mice to the permethrin-containing insecticide Ambush increased activities like chewing[13]; sublethal exposure of rats to permethrin increased aggressive behavior, agitation, and resistance to being captured[14]; and permethrin disrupted a learned feeding behavior in rats at doses of about 20 percent of the LD_{50}.[15]

Eye and skin irritation

Permethrin-containing products can be irritating to both eyes and skin. For example, the agricultural insecticide Pounce 3.2 EC "causes moderate eye irritation."[16] Ortho Total Flea Control 2 and Solaris Flea-B-Gon Total Flea Killer Indoor Fogger both cause "tearing, swelling, and blurred vision."[17,18] They also cause "redness, swelling, and possibly blistering" of the skin.[17,18] Adams 14 Day Flea Dip "causes eye injury"[19] and "may cause allergic reactions"[19] on skin.

Effects on the immune system

Experiments with laboratory animals indicate that the immune system (used by living things to defend themselves from disease) "appears to be a sensitive target for permethrin activity." Ingestion of permethrin reduces the ability of immune system cells called T-lymphocytes to recognize and respond to foreign proteins. Doses equivalent to 1/100 of the LD_{50}, inhibited T-lymphocytes over 40%. Permethrin ingestion also reduced the activity of a second type of immune system cell, natural killer cells, by about 40 percent.[20] In tests using mouse cell cultures, permethrin had similar effects on the immune system, inhibition of two kinds of lymphocytes.[21] Researchers concluded that "the immune system is exquisitely sensitive ... at exposure levels that cause no overt toxicity."[20]

Effects on reproduction

Permethrin affects both male and female reproductive systems. It binds to receptors for androgen, a male sex hormone, in skin cells from human males, causing researchers to "advise protection from any form of contact or ingestion of the pyrethroids."[22] Permethrin also binds to a different receptor, called the peripheral benzodiazepine receptor, that stimulates production of the male sex hormone testosterone.[23] In addition, permethrin caused reduced testes weights in a long-term feeding study of mice.[24] In females, permethrin exposure has caused embryo loss in pregnant rabbits[24] and in pregnant rats.[25]

Mutagenicity

Permethrin was mutagenic (damaging to genetic material) in three tests with human cell cultures, one with hamster cells, and one with fruit fly larvae. In cultures of human lymphocytes (white blood cells), permethrin exposure caused an increase in chromosome aberrations, chromosome fragments,[26] and DNA lesions.[27] In hamster ovary cell cultures, permethrin exposure caused chromosome aberrations.[28] Exposure to Ambush (a permethrin-containing insecticide) during larval development increased sex-linked lethal mutations in fruit flies.[29]

Carcinogenicity

According to the U.S. Environmental Protection Agency (EPA), permethrin is a possible human carcinogen (chemical that causes cancer).[30] EPA found that permethrin increased the frequency of lung tumors in female mice, and increased the frequency of liver tumors in male and female mice.[24] The World Health Organization reports that permethrin increased the frequency of lung tumors in females in two out of the three mouse studies it reviewed. Lung tumors increased with increasing permethrin exposure in the third study, but the increase was not statistically significant.[31]

There are no publicly available studies of the carcinogenicity of permethrin-containing insecticide products.

There are two molecular mechanisms which could explain permethrin's carcinogenicity. First, permethrin reduces the activity of an enzyme involved in the breakdown of the amino acid tryptophan. This can lead to the buildup of carcinogenic tryptophan breakdown products.[32] Second, permethrin inhibits what is called "gap junctional intercellular communication" (GJIC), chemical communication between cells. GJIC plays an important role in the growth of cells, and some cancer promoting chemicals inhibit GJIC.[33]

Other chronic effects

The liver is a sensitive target for permethrin effects. When EPA summarized 17 medium- and long-term laboratory studies that exposed rats, mice, and dogs to permethrin, effects on the liver were noted at the "lowest effect level" in all of them.[24] Other chronic effects in laboratory tests include enlarged adrenal glands at all doses tested in a rabbit feeding study, and increased kidney weights at all doses tested in a rat feeding study.[24]

Synergy

Synergy occurs between two or more chemicals when their combined exposure causes more adverse effects than the sum of their individual effects. A possible cause of the health problems reported by 30,000 veterans who served in the Persian Gulf War is exposure to a combination of chemicals, including permethrin.

The combination of permethrin, the anti-nerve gas drug pyridostigmine bromide, and the insect repellent DEET has been tested in laboratory animals. Neurotoxic symptoms, including decreased activity, diarrhea, shortness of breath, tremors, inability to walk, and damage to nerves, were observed in hens exposed to all three chemicals, but not in hens exposed to permethrin alone. Permethrin with just pyridostigmine bromide or just DEET also caused tremors and inability to walk, but symptoms were not as severe.[35]

Other pesticides interact synergistically with permethrin within

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other species. Permethrin and the herbicide atrazine synergistically induce growth of the soil fungus *Pythium ultimum*,[36] and permethrin and the insecticide amitraz are synergistically toxic to the bollworm.[37]

Individual susceptibility

Individuals vary in their susceptibility to permethrin, as has been illustrated by the following research:

- Based on tests with laboratory animals, it appears children may be more sensitive to permethrin than adults. Permethrin is almost five times more acutely toxic to eight-day-old rats than it is to adult rats.[38]
- Since sulfates are involved in one of the major pathways by which permethrin is broken down in humans, individuals with defects in sulfate-related enzymes may be unable to easily break down permethrin, leading to increased susceptibility to motor neuron disease.[39,40]
- Individuals with genetic variants of the enzyme pseudocholinesterase that have reduced activity are at higher risk of adverse effects from exposure to certain chemicals, including the permethrin combination implicated in symptoms seen in Gulf War veterans.[35]

It appears children may be more sensitive to permethrin than adults. Permethrin is almost five times more acutely toxic to eight-day-old rats than it is to adult rats.

Effects on nontarget animals

Beneficial arthropods: As a broad spectrum insecticide, it is not surprising that permethrin impacts beneficial arthropods, those that are useful in agriculture. Examples include the following:

- Permethrin is acutely toxic to honey bees; the median lethal dose is 0.008 micrograms per bee.[41] Sublethal exposures cause increased abnormal behavior (trembling, etc.), decreased foraging,[42] and impairment of bees' learning.[43]
- The International Organization for Biological Control tested the acute toxicity of permethrin to 13 species of beneficial arthropods and found that permethrin caused 99% mortality of 12 of the species, and over 80% mortality of the other. Effects were persistent, lasting over 30 days.[44] Sublethal doses also impact beneficial arthropods: permethrin inhibited the emergence of a parasitoid wasp from eggs of the rice moth *Corcyra cephalonica*[45] and disrupted the foraging pattern of another parasitoid wasp as it searched for its aphid prey.[46] (Parasitoids are insects that lay their eggs in, on, or near their prey. The eggs hatch and the larvae consume the prey as they develop. They often keep populations of agricultural pests at low levels.)

Aquatic insects: Because it is a broad spectrum insecticide, permethrin has severe impacts on aquatic insects. Permethrin applications to forest streams caused "a major increase in the density of drifting invertebrates" described as "catastrophic." (Drifting animals are those that are sufficiently poisoned by the insecticide that they are washed downstream.) Most applications were also followed by "rapid depletion of bottom fauna," insects that live in the stream bed; recovery required between 1 and 18 months.[47] Mayflies and damselflies are the most sensitive species.[49] Permethrin also bioconcentrates in aquatic insects; bioconcentration factors in stoneflies ranged from 43 to 570.[49]

Birds: While permethrin's acute toxicity to birds is low,[50] it causes other adverse effects. Three-week dietary exposure of chickens reduced hemoglobin (oxygen carrying protein) levels, and red blood cell counts, while increasing the number of white blood cells.[51] The reduction in hemoglobin occurred at the lowest dose tested, 33 mg/kg.[51] Permethrin also caused decreased immune responses in chicks,[52] and damaged mallard ovaries.[53]

Fish: Permethrin is highly toxic to fish. This toxicity is due, in part, to the sensitivity of their nervous system.[54] Fish also lack the enzymes that break down permethrin in other animals.[55] The LC_{50} (the concentration that kills 50 percent of a population of test animals) is less than one part per million (ppm) for almost all fish species tested, and for some fish is less than 1 part per billion (ppb). Agricultural permethrin products called emulsifiable concentrates are about twice as toxic to fish as permethrin alone. Small fish are less tolerant of permethrin than large fish, and it is more toxic in cold water than in warm water.[56] Fish also have a particular developmental stage when they are most susceptible.[57]

Sublethal effects on fish include abnormal swimming, a reduced startle response, and loss of equilibrium.[58] Permethrin bioconcentrates in fish, so that concentrations in fish are higher than the concentration in the water in which the fish live. Bioconcentration factors (the ratio between the concentration in the fish and the concentration in the water) up to 113 have been measured in brook trout,[59] up to 613 in Atlantic salmon,[59] and up to 631 in rainbow trout.[60]

Complex effects of permethrin on fish have been documented by the Canadian Forest Service in field studies. They found that diets of trout and salmon were altered when permethrin killed the insects these fish use as food. In some cases, diets were altered for a year following treatment. Reductions in fish growth rates, and migration to untreated areas followed; recovery required four months. The researchers concluded that permethrin is "not an acceptable treatment for large-scale use in forest areas containing fish-producing water."[61]

Amphibians: Permethrin disrupts the growth and development of tadpoles. Exposure slowed growth for two to three weeks, and increased the frequency of a tail abnormality. The increase in this deformity occurred at the lowest concentration

of permethrin tested, 0.1 ppm. At this concentration tadpoles also responded to prodding in a jerky and disorganized way, making them vulnerable to predation. Tadpoles exposed to an even lower concentration (0.05 ppm) reduced their feeding for several weeks after exposure.[62]

Permethrin also effects brain function in tadpoles. Concentrations of 0.25 ppm decreased the amounts of two specific proteins in the brain, while increasing the total amount of protein. One of the proteins is associated with learning. Activity of several nervous system enzymes, including acetylcholinesterase, decreased.[63]

Other aquatic animals: Permethrin is very highly toxic to lobster; the LC_{50} is less than 1 ppb.[64] It is highly toxic to oyster larvae, with an EC_{50} (the concentration causing abnormal development in half of the larvae) of less than 1 ppm.[65]

Permethrin bioconcentrates in oysters, with a bioconcentration factor of 1900.[66] Water fleas are also very sensitive to permethrin exposure; LC_{50}s of several species are about 1 ppb.[67] Permethrin also caused "severe mortalities" of two kinds of zooplankton, cladocerans and copepods with recovery taking about three months.[68]

Mysid shrimp are killed by permethrin at concentrations so low that they cannot be detected in water (the LC_{50} is 0.02 ppb). This means that "any detection of these insecticides in estuarine waters would likely be associated with adverse effects."[66] Another animal that is very sensitive to permethrin is crayfish; LC_{50}s for the red swamp crayfish vary from 0.4 to 1.2 ppb. Researchers concluded that "even the lowest operational treatment level used for insect management would seriously impact crayfish populations."[67]

Residues on food

The Food and Drug Administration's (FDA) monitoring program routinely finds permethrin on food. In 1996, it was the 13th most commonly detected pesticide.[68] Similar results were found in monitoring of 14 fruits and vegetables by the U.S. Department of Agriculture; permethrin was the tenth most frequently detected pesticide and was often found on spinach (60% of the samples tested) and tomatoes (11% of the samples tested).[69] Permethrin was also frequently found on celery and lettuce.[70]

Permethrin has also been found in baby food: FDA's 1996 monitoring found it in 12% of the samples tested. The Environmental Working Group found permethrin was the most commonly detected pesticide in peach baby food (44% of the samples tested) and was also found in plums (11% of the samples tested).[71]

Contamination of water

Permethrin has been found in ground and surface water. The U.S. Geological Survey has found permethrin in streams and rivers in the Mississippi River Basin,[72] the Central Columbia Plateau (Washington and Idaho),[73] the Georgia-Florida Coastal Plain,[74] the San Joaquin-Tulare Basin (California),[75] and the Ozark Plateau (Arkansas and nearby states).[76] Permethrin has also been found in groundwater in Virginia.[76]

Source: Pages 49-52 of this publication are drawn from Global Pesticide Campaigner, December 1999, Vol. 9, No. 3. Published by Pesticide Action Network-NA, San Francisco, USA

Drift

Drift, pesticide movement during application away from the target area, has been measured for two types of permethrin applications: aerial and back pack mistblower. Aerially applied permethrin drifted 180-240 meters (590-790 feet) under conditions "highly conducive" to drift.[78] These researchers suggested using buffers of 150 meters (490 feet). Back pack mistblower applications of permethrin drifted 150 meters.[79]

Persistence

According to EPA, permethrin's half-life (the amount of time required for half of the original amount of a chemical to break down or move away from the study site) was 17 days in a North Carolina agricultural soil and 43 days in Illinois.[80] When used as a termiticide, permethrin persists longer; soil concentrations did not decline during the first year.[81] Permethrin also persists longer in tree needles, foliage, and bark, up to 363 days.[82] The ability of permethrin to persist in the environment was graphically illustrated by a study of an application of permethrin ear tags to cattle. Permethrin was found on all surfaces analyzed, not only on the cattle, but also on the bark of trees in their pasture, on a fence pole, and in grass. Some residues were found three months after the ear tags were applied.[83]

Resistance

Resistance (the evolution of a strain of insect that is able to tolerate a particular insecticide) to permethrin has been documented in a wide variety of insects. These species include pear psylla,[84] fall armyworm,[85] German cockroach,[86] spotted tentiform leafminer,[87] diamondback moth,[88] house fly,[89] stable fly,[90] head lice[91-93] and tobacco budworm.[94] Many of these species are resistant to other synthetic pyrethroids as well as permethrin. The level of resistance is less than tenfold in some of the species but high levels of resistance have been observed in cockroaches (45-fold),[86] lice (up to 385-fold)[91] and budworm (1400-fold).[94]

Inert ingredients

Like most pesticide products, permethrin insecticides contain ingredients that are typically claimed as trade secrets by pesticide manufacturers. Limited information about "inerts" in permethrin products is available. Examples include:

- **Xylenes** are in the agricultural insecticides Pounce 3.2 EC,[16] Ambush 2E,[95] and Ambush 50.[96] Xylenes cause eye and skin irritation, headaches, nausea, confusion, tremors, and anxiety in exposed humans. In laboratory tests, xylenes have caused kidney damage, fetal loss, and skeletal anomalies in offspring.[97]
- **Methyl paraben** is in the head lice cream rinse Nix,[98] regulated as a drug, not as a pesticide. Methyl paraben is a skin sensitizer, and causes eye, skin, digestive, and respiratory irritation.[99]
- **Dimethyl ether** is in the household insecticides Flea-B-Gon Total Flea Killer Indoor Fogger[17] and Ortho Total Flea Control 2.[18] It causes respiratory, skin, and eye irritation and depresses the central nervous system. It is also a severe fire hazard.[100]
- **Butane** is in the household insecticides Raid Yard Guard Outdoor Fogger V and Off Yard and Deck Area Repellant 1.[101,102] It is "extremely flammable" and short-term exposure causes irritation, nausea, drowsiness, convulsions and coma.[103]

Diazinon: Toxicology

A factsheet by the Northwest Coalition for Alternatives to Pesticides (NCAP).

- **Diazinon is an organophosphate insecticide with agricultural, commercial, and household uses. Household uses predominate, with 75 million applications in the U.S. annually totalling over five million pounds.**

- **Diazinon is toxic to the nervous system. Symptoms of acute diazinon poisoning include headache, nausea, dizziness, tearing, and sweating. Some symptoms, including blurred vision, headaches, and memory problems, can last for months or years.**

- **In laboratory tests, feeding diazinon to pregnant animals has caused a decrease in the endurance, coordination, and growth of their offspring. In addition, the sexual development of offspring of both sexes was delayed.**

- **Diazinon exposure has been associated with an increased risk of brain cancer in children and the cancer non-Hodgkin's lymphoma in farmers.**

- **Infants are especially susceptible to diazinon. In addition, 9–16% of people have a slow form of an important detoxification enzyme and thus are particularly susceptible.**

- **The U.S. Environmental Protection Agency estimated exposure to household residents following use of diazinon insecticide products and found that exposure following lawn care applications of liquid products and following indoor applications exceed the agency's "levels of concern."**

By Caroline Cox

Diazinon (see Figure 1) is an organophosphate insecticide, chemically related to other common insecticides like malathion and chlorpyrifos.[1] It was first registered in the U.S. in 1956[2] and is sold under a variety of brand names, including DZN[3] and Knox Out 2FM.[4]

Use

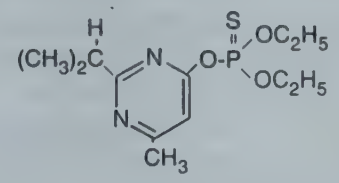
Diazinon has agricultural, commercial, and household uses, but household uses predominate. Estimated agricultural use is 1.5 million pounds annually. Crops using the most diazinon are almonds, berries, pecans and nectarines.[5] About 75 million household applications are made annually, 18 million indoors and 57 million outdoors.[6] Home, lawn and garden use totals 5.5 million pounds per year.[5]

Mode of action

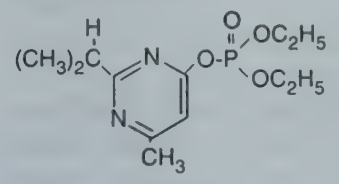
Inside living things, diazinon is transformed into a molecule called diazoxon. (See Figure 1) Diazinon, and the more potent diazoxon,[7] kill insects by interfering with nervous system function, as do all members of the organophosphate chemical family. Normally, impulses are transmitted chemically from the end of one nerve cell to the beginning of another; one of the chemical transmitters used in animal nervous systems is called acetylcholine. After transmitting the nerve impulse, acetylcholine is destroyed by an enzyme called acetylcholinesterase (AChE) in order to clear the way for another transmission. Organophosphates attach to AChE and prevent it from destroying acetylcholine, causing overstimulation of the nerves.[8]

Source: Pesticide Action Network-NA, San Francisco, USA

Figure 1
Diazinon and Diazoxon



diazinon
(O,O-diethyl O-(2-isopropyl-6-methyl-4-pyrimidinyl)phosphorothioate)



diazoxon

Mammal and insect nervous systems are similar enough that effects of organophosphates are similar.[1]

It is worth noting that not all of diazinon's toxicological effects stem from its inhibition of AChE. Diazinon and other organophosphates inhibit numerous enzymes with molecular structures that are similar to AChE. For example, an enzyme involved in the metabolism of the amino acid tryptophan is strongly inhibited by diazinon and diazoxon.[9]

Inert ingredients

Like most pesticide products, most commercial diazinon products contain ingredients other than diazinon that are misleadingly labelled as "inert." Public information about the identity of these inerts is scanty.

Effects of acute exposure

Symptoms of acute (short-term) diazinon poisoning in people are similar to the symptoms of any organophosphate insecticide poisoning: headache, nausea, dizziness, tearing, sweating, salivation,[1] drowsiness, agitation, anxiety,[10] and influenza-like symptoms.[11] Symptoms of higher exposure include an abnormal heart rate (either too slow or too rapid),[12] muscle weakness, muscle twitching, pinpoint pupils,[1] lung congestion,[13] cardiac arrest,[14] and seizures.[15]

Other symptoms observed in laboratory animals after acute exposure include abnormal walking, reduced activity,[16] increased blood sugar levels,[17] low blood pressure,[18] and inflammation of the pancreas.[19]

Physicians have reported that symptoms of acute diazinon exposure in children are different than those in adults. Tearing, sweating,[1] slow heart rate and muscle twitches,[20] common in adults, are infrequent in children. Seizures are much more common in children than in adults.[20] Inflammation of the pancreas is another symptom that is "not rare" in children with diazinon poisoning.[21]

Whether acute exposure to diazinon and other organophosphate insecticides can cause long-term health problems has been a controversial issue. Recently (1998), however, a U.S. Environmental Protection Agency (EPA) review found that "symptoms may persist for months or years after the initial exposure."[22] Persistent symptoms include blurred vision, headaches, muscle weakness, lethargy, short term memory impairment, inability to concentrate, confusion, lowered intelligence test scores, depression, and irritability.[23]

Skin allergies

Both diazinon and the diazinon-containing insecticide Diazinon 4E caused allergic skin reactions in people. Although pesticides in general are tested on laboratory animals, diazinon and Diazinon 4E were tested on a group of 56 people. About 10% of them showed "positive dermal sensitization."[24] In this test, diazinon is applied to the skin of the subjects twice. If the reaction to the second exposure is greater than the reaction to the first exposure, the chemical causes sensitization.[25]

Effects of subchronic and chronic exposure

Laboratory studies of subchronic (medium-term) and chronic (long-term) exposure typically expose animals by feeding them the test chemical over a period of several months for subchronic tests, or over a one to two year period for chronic tests. In subchronic and chronic tests with diazinon, the primary effect studied is inhibition of acetylcholinesterase (AChE), diazinon's target enzyme. In five studies (a six-week study of people; a one-year, a three-month, and a one-month study of dogs; and a one-month study of female rats) AChE inhibition occurred at strikingly low doses: the animals were fed less than 50 micrograms per kilogram of animal body weight per day.[26, 27, 28]

A study of rats that were exposed by breathing diazinon-contaminated air measured AChE inhibition at a similar level of exposure (26 micrograms per kilogram (µg/kg) of body weight per day).[29]

At somewhat higher feeding levels (500 µg/kg per day), other effects occur. Two studies from Simon Fraser University found that medium-term exposure caused reduced weight gain, liver injury, and reduced levels of four chemicals (other than acetylcholine) that are used to transmit nervous system impulses in the brain.[30, 31]

For pets, one form of chronic exposure is from wearing flea collars. Several studies have shown that the activity of acetylcholinesterase was inhibited in dogs and cats wearing flea collars. Inhibition continued for the entire time the collar was worn, up to 315 days.[32]

Recently, a U.S. Environmental Protection Agency review found that "symptoms may persist for months or years after the initial exposure."

Only four of the above studies, the tests of flea collars on pests and the one-month study of people, used commercial diazinon-containing products.

Effects on reproduction

Diazinon exposure of pregnant animals in laboratory tests has demonstrated that this insecticide can cause a variety of reproductive problems, including damage to the developing nervous system, delays in sexual development, stillbirths, death of newborn offspring, and birth defects.

The effects on the developing nervous system are most significant. An EPA-funded study using mice exposed to low levels of diazinon in their food (0.18 milligrams per kilogram, mg/kg, per day) found that the endurance and coordination of the offspring was impaired. They were unable to remain on as steep of an inclined plane as mice born to unexposed mothers. In addition, their ability to climb developed later than mice born to unexposed mothers.[33]

This study also showed that diazinon exposure of pregnant mice delayed the sexual development of their offspring. Sexual maturity (measured by the age when vaginal opening occurred in females and descent of the testes in males) was delayed about 6% in offspring of exposed mothers.[33]

A study of dogs that were fed diazinon (1 mg/kg per day) during pregnancy showed that their exposure increased the number of stillbirths. Less than 6% of the offspring of unexposed mothers were stillborn, while 15% of offspring of mothers fed diazinon were stillborn. The researchers who conducted this study, from the Food and Drug Administration, noted that diazinon made the mothers "extremely high strung"[34] resulting in stillbirths as the mothers "would not lay still while giving birth."[34]

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These researchers also found that feeding diazinon (5 mg/kg per day) to pregnant pigs increased the incidence of skull deformities in the offspring.[34]

Finally, a study of pregnant rats fed diazinon (7 mg/kg per day) found that the number of offspring that died was greater in litters from exposed mothers than for litters from unexposed mothers. The offspring of exposed mothers also grew more slowly while they were nursing. This study was conducted by a diazinon manufacturer.[35]

Diazinon also has caused reproductive problems in male animals. Dogs fed diazinon (20 mg/kg per day) developed atrophied testicles.[36]

There is no publicly available information about the reproductive effects of commercial diazinon-containing products.

One of diazinon's break down products, monothiotepp, has been reported to be 14,000 times more toxic than diazinon itself.

Endocrine disruption

Problems caused by synthetic chemicals that disrupt the normal functioning of our hormone systems have been well publicized in the last decade. Of particular concern are chemicals that interfere with the activity of estrogen, often called the female sex hormone. Estrogen has recently been shown to affect the development and growth of cells in the lining of the colon. The result of abnormal growth of these cells is colon cancer. In tests with cultures of cells from a human colon, low concentrations of diazinon had growth-promoting effects, suggesting diazinon had interfered with the normal activity of estrogen.[37]

There is no publicly available information about the endocrine-disrupting effects of commercial diazinon-containing products.

Carcinogenicity

Diazinon's carcinogenicity (its ability to cause cancer) has been studied in laboratory animals with negative results; as a result it has been classified as "not likely" to be a carcinogen by EPA.[38]

Studies of people who have used diazinon, however, show just the opposite: there is an association between diazinon use and the risk of certain types of cancer. In a study of children in Missouri, garden diazinon use by the parents was associated with an increased risk of brain cancer in their children.[39] In a study of Iowa and Minnesota farmers conducted by the National Cancer Institute (NCI), use of diazinon was associated with an increased risk of non-Hodgkin's lymphoma.[40] Similar results were found in an NCI study of Nebraska farmers.[41]

Mutagenicity

Diazinon's mutagenicity, its ability to cause genetic damage, is controversial. The World Health Organization, in its review of the effects of diazinon on human health and the environment, wrote that diazinon "gave no evidence of a mutagenic potential."[42] However, a series of other studies show that diazinon in fact can damage genes in human blood cells, in cells from laboratory animals, and in bacteria.

A study conducted by Italian cancer researchers used concentrations of diazinon equivalent to those found in an Italian food monitoring study. They found that this low level of exposure increased the occurrence in human blood cell cultures of a type of genetic damage called micronuclei.[43] Micronuclei are broken or separated chromosomes produced when a cell divides.[44] Micronuclei were about 50% more frequent in exposed cells than in unexposed cells.[43]

Two older studies of human blood cell cultures found that diazinon was mutagenic. Abnormal chromosomes were more frequent in human blood cell cultures exposed to diazinon than they were in unexposed cells,[45] as was a type of genetic damage called sister chromatid exchanges.[46] (Sister chromatid exchanges are exchanges of genetic material between parts of a duplicating chromosome.[47])

A fourth study, conducted by the National Institute of Hygenic Sciences in Japan, found that diazinon exposure increased the frequency of abnormal chromosomes in hamster lung cell cultures.[48]

Finally, a study of *Salmonella* bacteria found that diazinon was mutagenic to one of the four strains tested.[49]

There is no publicly available information about the mutagenicity of commercial diazinon-containing products.

Sensitive populations

Physicians have long noted that infants appear to be particularly susceptible to diazinon poisoning. For example, in 1970, three-week old twins were poisoned by a diazinon cockroach treatment in the other half of the duplex in which they lived. Both twins required five days of hospitalization, although none of the adults or older children living in either half of the duplex were ill.[50] In another example, a two-month old infant developed symptoms of cerebral palsy after a diazinon treatment of her home. Symptoms persisted for seven months, until her family moved out of the treated home.[51, 52] One reason for infants' increased susceptibility is that newborns have low levels of the enzyme that usually breaks down diazoxon, the active form of diazinon.[53]

Individuals whose body chemistry is less efficient at breaking down diazoxon are also more sensitive to this insecticide. The enzyme that breaks down diazoxon is produced by a gene called PON1. Each person has two PON1 genes. One form of this gene, called the R form, produces an enzyme that is less efficient at breaking down diazoxon, so people with two R genes are most susceptible to diazinon. About 9% of people of northern European descent have two R genes, while about 16% of people of Hispanic origin have two R genes. This means that a substantial fraction of the population will be particularly sensitive to diazinon and suggests an additional hazard for farmworkers, since in the U.S. many farmworkers are of Hispanic origin.[54]

Another sensitive population may be those who are malnourished. Studies with laboratory animals have found that rats fed a protein deficient diet were almost twice as susceptible to diazinon as rats fed an adequate diet.[55,56]

Toxic breakdown products

If a diazinon-containing product is contaminated with a trace of water, some of the diazinon in the product breaks down into two chemicals that are extremely potent acetylcholinesterase inhibitors, monothiotepp and sulfotepp. Monothiotepp has been reported to be 14,000 times more toxic than diazinon itself. In the early 1990s, when several Australian dogs died after being washed with a diazinon product and some of their handlers became ill, regulatory authorities suspected monothiotepp or sulfotepp contamination and screened diazinon-containing products from pesticide retailers. They tested 169 products and found that about 5% were contaminated with the two breakdown products and traces of water.[57] The contamination of these products greatly increases their toxicity. NCAP located no similar studies of U.S. products.

A review of data collected by poison control centers nationwide between 1985 and 1992 showed that diazinon was the second most frequent cause of nonoccupational insecticide poisonings.

Exposure

Exposure to diazinon is a complicated subject. "Organophosphates are efficiently absorbed by inhalation, ingestion, and skin penetration,"[1] according to EPA, and exposure by "multiple routes can lead to serious additive toxicity."[1] For exposures following residential applications, a single application can lead to exposure via all three routes.[58]

For example, researchers from British Columbia and from North Carolina State University studied broadcast applications to carpets and "crack and crevice" applications, thin streams of pesticide applied just to the kind of site usually inhabited by cockroaches. (Crack and crevice applications are an alternative to broadcast sprays and in general use a smaller amount of insecticide.) After application, diazinon was found both in the air of the treated rooms and on horizontal surfaces in the rooms.[59-61] Diazinon in air leads to inhalation exposure. Diazinon settling on horizontal surfaces leads to both exposure through the skin (if people contact the horizontal surfaces) and ingestion (if, for example, a hand contacts a contaminated surface and then is put in the mouth).

These exposures can be persistent. Air was contaminated for 21 days following crack and crevice application,[59] horizontal surfaces were contaminated for six weeks following application.[60] The British Columbia researchers recommended not entering any unventilated rooms for at least two days after treatment.[61]

EPA surveys of air inside houses, not specifically ones recently treated with diazinon, found that diazinon is surprisingly common in indoor air. In surveys in Florida,[62] Texas,[63] and Arizona,[64] between 53% and 100% of homes were contaminated with diazinon.

Outdoor applications also lead to exposure through inhalation (breathing of contaminated air), dermal (skin contact with treated turf), and ingestion (inadvertent hand-to-mouth transfers).[65]

EPA recently (April 2000) estimated exposure via multiple routes following both lawn care and crack-and-crevice indoor applications. They found that exposures following lawn care applications of liquid diazinon products and following indoor crack and crevice treatments exceeded EPA's "level of concern" for both adults and children.[66]

Contaminated house dust has recently been studied and can also result in multiple routes of exposure. Skin can contact dust particles, the particles can be inhaled and they can be ingested.[67] Dust is believed to be a particularly important source of exposure to children.[68]

Diazinon-contaminated dust can be common. Surveys in Florida, New Jersey, California, Texas and Arizona found diazinon in the dust from 53% to 80% of the houses tested.[63,64,68-70]

Farmworker children may be particularly at risk of exposure to diazinon via dust. The California study found higher and more frequent diazinon contamination in farmworker homes than in non-farmworker homes in the same town.[70]

Human poisonings

Diazinon's frequent use and significant toxicity means that poisonings of people are frequent. EPA characterizes diazinon as "one of the leading causes of acute reactions to insecticide use reported as poisoning incidents in the United States."[71] A review of data collected by poison control centers nationwide between 1985 and 1992 showed that diazinon was the second most frequent cause of nonoccupational insecticide poisonings. Almost one-quarter of the insecticide poisonings reported to the centers were caused by diazinon. Nearly half of these poisonings involved children under six years of age.[72]

Effects on birds

Acute toxicity: Diazinon is notorious because of its acute (short-term) toxicity to birds. For many species, its acute toxicity is less than 10 mg/kg, placing it in the EPA's highest acute toxicity category. Sensitive species include Canada goose, house sparrow, mallard duck, bobwhite quail, red-winged blackbird,[73] and American wigeon.[74]

Symptoms of acute poisoning in birds are lack of coordination, wing spasms, diarrhea, salivation, and seizures.[75]

Diazinon-related bird kills are common. According to EPA, "Diazinon has caused widespread and repeated mortality of

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birds."[76] Only the carbamate insecticide carbofuran has caused more pesticide-related bird kills than diazinon.[77] These hazards led to cancellation of diazinon's uses on golf courses and sod farms, where diazinon-caused bird kills were frequent, in 1988.[78] Even though these uses have ended, EPA's incident reporting system indicates that the number of diazinon-caused bird kills has increased steadily since the 1980s.[77]

Both liquid and granular diazinon products are hazardous to birds. Liquid products leave residues on vegetation, which can then be eaten by birds. Diazinon also washes into puddles during rainfall or irrigation, and birds drink the contaminated water. Birds eat granular products when they stick to food or pick them up directly as grit.[79] A single diazinon granule has killed house sparrows in laboratory tests, and five granules have killed blackbirds.[80]

According to EPA, "Diazinon has caused widespread and repeated mortality of birds."

EPA's assessment of diazinon's acute risks to birds concluded that the agency's "levels of concern"[81] were exceeded for all uses evaluated. EPA stated that its past efforts to mitigate these risks by lowering application rates and adding label warnings "are not adequate to prevent mortality."[82]

Problems with reproduction: In addition to its acute toxicity, diazinon reduces the reproductive success of birds. Examples include the following problems:

- *A decrease in the successful hatching of eggs.* Robin eggs in Christmas tree plantations sprayed with diazinon hatched at a lower rate than did eggs in unsprayed nests.[83] In a laboratory study, the hatching rate of eggs from chickens fed 0.1 ppm in their food was 87%, compared to 94% from birds fed uncontaminated food.[84]
- *A decrease in the survival of nestlings.* Mortality of song sparrow nestlings in Christmas tree plantations sprayed with diazinon was greater than mortality in unsprayed nests.[83] In a laboratory study, survival of mallard ducklings whose mothers were fed 16 ppm of diazinon in their food was significantly less than the survival of ducklings whose mothers were fed uncontaminated food.[85]
- *A decrease in the number of eggs laid.* The number of eggs produced by bobwhite quail fed 35 ppm of diazinon in their food was reduced compared to quail fed uncontaminated food.[86]
- *An increase in the number of deformities in developing chicks.* Injection of small amounts of diazinon (6.25 micrograms (μg) into developing eggs caused the chicks to develop twisted necks.[87] Higher amounts of diazinon caused additional defects in quail and chicken including folding of the spinal cord,[87] shortening of the neck,[87] fusing and twisting of vertebrae,[88] abnormal development of ribs and breastbone,[88] reduced calcification of bones,[89] curled claws,[90] and reduced growth of leg and wing bones.[90]

Endangered species: EPA's assessment of diazinon's hazards concluded that the agency's "levels of concern" for endangered bird species were exceeded by all the uses of diazinon evaluated, including liquid and granular diazinon products used in both agricultural and urban settings.[91] These concerns are supported by a study of loggerhead shrikes in Virginia. Diazinon contaminated 29% of the kidney, liver, and brain samples tested.[92]

Exposure: Studies of diazinon exposure to birds are rare. However, the few studies obtained by NCAP indicate that diazinon exposure could be widespread. In California's Central Valley, diazinon was found on the feathers of 45% of the hawks studied.[93] Diazinon also was found in a goose that died after a condominium lawn was treated with diazinon.[94]

Lack of ability to detoxify organophosphates: Birds have lower levels of a group of enzymes used to break down diazinon than do mammals.[95] According to researchers, "this appears to be the main reason why birds are much more susceptible than mammals"[95] to diazinon and related insecticides.

Special susceptibility of juveniles: Young birds appear to be more susceptible to diazinon poisoning than mature birds. In a study of starlings, newly hatched nestlings were 20 times more sensitive than birds that had fledged.[96]

Effects on fish

Acute toxicity: According to EPA, diazinon is highly toxic (median lethal concentration, LC_{50}, less than 1 ppm) or very highly toxic (LC_{50} less than 0.1 ppm) to about 60% of the fish species for which the agency has data. These include bluegill sunfish; brook, cutthroat, lake, and rainbow trout; and striped mullet.[97] Fish species that are sensitive to diazinon have enzymes that activate diazinon more quickly, enzymes that break it down more slowly, or nerves that are more affected by diazinon.[98]

EPA has calculated that acute risks to fish from diazinon's use on urban lawns and many of its agricultural uses exceed the agency's "levels of concern."[99]

Genetic damage: Diazinon has caused genetic damage in the central mudminnow, a fish used as a model for testing of genetic effects. In aquarium studies, diazinon at the low concentration of 160 parts per trillion caused an increase in genetic damage called sister chromatid exchanges (SCEs),[100] exchanges of genetic material between parts of a chromosome as it duplicates.[101]

Effects on reproduction: Diazinon can disrupt the physiology of reproducing fish. Male Atlantic salmon returning to spawning streams normally react to the smell of urine from female salmon who have recently ovulated. In response to this smell, the levels of sex hormones in males' blood rise and their production of milt (sperm) increases. Concentrations of diazinon above 300 ppt reduced these responses.[102]

Diazinon also impaired reproduction at only slightly higher concentrations (560 ppt) in a study of sheepshead minnows.[103] Reproduction was impaired during diazinon exposure and for up to a month after exposure. In a study of brook trout,

diazinon reduced growth of offspring at concentrations of 550 ppt.[104]

Effects on antipredator behavior: A study by the National Marine Fisheries Service found that diazinon affects the behavior of young chinook salmon. Concentrations (1 and 10 ppb) which "emulate diazinon pulses in the natural environment"[105] affect the olfactory system (sense of smell) and disrupt antipredator behaviors that are normally initiated when the fish smell alarm chemicals given off by other fish in the water.[105]

Bioconcentration: Diazinon bioconcentrates in fish, meaning that the concentration in fish is greater than that in the water in which the fish lives. Bioconcentration factors (the ratio between the concentration in the fish and that in the water) vary from 18 to 300.[106-110]

Damage to gills: Concentrations of diazinon as low as 15 ppb have damaged gills of the bluegill sunfish. At higher concentrations, diazinon "may result in severe physiological problems, ultimately leading to the death of fish."[111] Gills may be particularly susceptible to diazinon because diazinon bioconcentrates more strongly in gills (bioconcentration factor 2300)[112] than in some other fish tissues.[113]

Liver damage: Diazinon also bioconcentrates in the liver, where factors as high as 1850 have been measured.[114] In the livers of exposed fishes, concentrations of 150-200 ppb cause cell membranes to rupture[115] and cavities to form.[115, 116]

Effects on vision: Exposure of eggs to diazinon causes areas of dead cells to form in the retina of developing medaka.[117]

Hazards to endangered species: EPA's risk assessment considered 19 agricultural uses and one household use (broadcast treatment of lawns). The agency's "levels of concern" for endangered freshwater and marine fish species were exceeded by all 20 uses evaluated.[99]

Caroline Cox is editor of the Journal of Pesticide Reform (JPR), *a publication of the Northwest Coalition for Alternatives to Pesticides (NCAP).*

This information originally appeared in JPR 2000 Summer and Fall issues. To find out more about NCAP and the Journal of Pesticide Reform, *visit their Web site at http://www.pesticide.org. NCAP, P.O. Box 1393, Eugene, Oregon 97440-1391; phone (541) 344-5044; email info@pesticide.org.*

Source: Pages 53-58 of this publication are drawn from Global Pesticide Campaigner, December 2000, Vol. 10, No. 3. Published by Pesticide Action Network-NA, San Francisco, USA

Triclopyr

A factsheet by the Northwest Coalition for Alternatives to Pesticides (NCAP)

- Triclopyr is a broadleaf herbicide used primarily on pastures, woodlands, and rights of way. Garlon 3A and Garlon 4 are brand names of common triclopyr herbicides. Two forms of triclopyr are used as herbicides: the triethylamine salt (found in Garlon 3A) and the butoxyethyl ester (found in Garlon 4) .

- The amine salt of triclopyr is corrosive to eyes. Both the amine salt and the ester are sensitizers and can cause allergic skin reactions.

- In laboratory tests, triclopyr caused an increase in the incidence of breast cancer as well as an increase in a type of genetic damage called dominant lethal mutations. Triclopyr also is damaging to kidneys and has caused a variety of reproductive problems.

- The ester form of triclopyr is highly toxic to fish and inhibits behaviors in frogs that help them avoid predators. Feeding triclopyr to birds decreases the survival of their nestlings.

- Triclopyr inhibits the growth of mycorrhizal fungi, beneficial fungi that increase plants' ability to take up nutrients. Triclopyr also interferes with one step in the process by which atmospheric nitrogen is transformed by microorganisms into a form that is usable by plants.

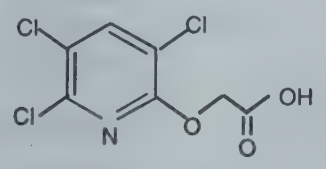
- Triclopyr is mobile in soil and has contaminated wells, streams, and rivers. Contaminated water has been found near areas where triclopyr is used in agriculture, in forestry, on urban landscapes, and on golf courses.

- The major breakdown product of triclopyr (3,5,6-trichloro-2-pyridinol) disrupts the normal growth and development of the nervous system. In laboratory tests, it also accumulates in fetal brains when pregnant animals are exposed.

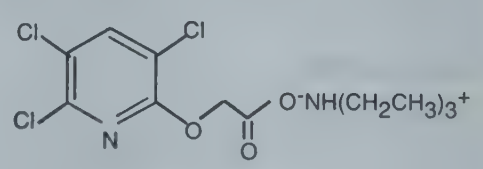
By Caroline Cox

Triclopyr is a selective herbicide used to kill unwanted broadleaf plants. Triclopyr herbicides contain one of two forms of triclopyr, either the triethylamine salt or the butoxyethyl ester. (See Figure 1.) Triclopyr was first registered as a pesticide in the U.S. in 1979, and its major manufacturer is Dow AgroSciences.[1] It is sold under a variety of trade names, including Garlon 3A,[2] Garlon 4,[3] Pathfinder,[4] Remedy,[5] Turflon,[6] and (in Canada) Release.[7] Garlon 3A contains the triethylamine salt, the others contain the butoxyethyl ester.[2-7] Triclopyr is in the carboxylic acid chemical family.[8]

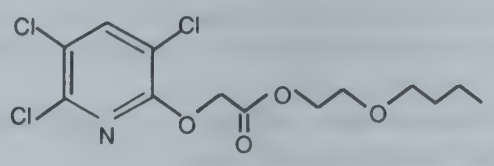
Figure 1
Triclopyr, Its Triethylamine Salt, and Its Butoxyethyl Ester



triclopyr ((3,5,6-trichloro-2-pyridinyl)oxy)acetic acid



triethylamine salt of triclopyr



butoxyethyl ester of triclopyr

Use

According to estimates from the U.S. Environmental Protection Agency (EPA), use of triclopyr in the U.S. totals almost 700,000 pounds per year.[9] Pastures, woodlands, and rights of way account for almost three-quarters of this use, while rice is the major agricultural use.[9] An estimated 455,000 applications are made annually to U.S. lawns and yards.[10]

How Does Triclopyr Kill Plants?

Triclopyr imitates a plant hormone called indoleacetic acid, one of a number of plant hormones classified as auxins. Triclopyr causes the growing tips of the plant to elongate, followed by distortion, withering, and the death of the plant.[8]

Source: Pesticide Action Network-NA, San Francisco, USA

Triclopyr is selective (most toxic to broadleaf plants) because grasses are quickly able to transform triclopyr into compounds that do not have hormonal activity.[11]

"Inert" Ingredients in Triclopyr-Containing Products

According to U.S. pesticide law, any ingredients in triclopyr herbicides other than triclopyr are called "inert."[12] Except for acute toxicity testing, all toxicology tests required for registration as a pesticide were conducted with triclopyr, not the combination of ingredients found in commercial products.[13] "Inert" ingredients used in triclopyr herbicides include the amine salt of dodecylbenzenesulfonic acid[14], ethanol,[2] ethylenediamine tetraacetic acid,[2] a petroleum solvent[14] containing kerosene,[3,5-7] polyglycol,[15] ethoxylated sorbitan monooleate,[14] and triethylamine.[2]

Acute Toxicity

Symptoms of short-term exposure to triclopyr include lethargy incoordination, weakness, difficult breathing, and tremors. Anorexia and diarrhea have also been observed in animals exposed to triclopyr.[16]

EPA classifies the triethylamine salt of triclopyr in the agency's highest acute toxicity category for eye irritation. It is "corrosive" to eyes with damage lasting over three weeks. Both the amine salt and the butoxyethyl ester sensitize skin,[17] so that subsequent exposures cause greater allergic reactions than the first exposure.[18]

Subchronic Toxicity

In a subchronic (medium-term, 3 month) laboratory feeding study with rats, triclopyr caused kidney damage (degeneration of tubules). This damage was observed at doses of 20 milligrams per kilogram (mg/kg) of body weight per day.[19]

There are no publicly available subchronic toxicity studies of commercial triclopyr-containing products.

Chronic Toxicity

In a chronic (long-term) laboratory feeding study, rats fed triclopyr developed kidney damage more often than unexposed rats. In a long-term study using dogs, the animals which were fed triclopyr gained less weight, had less hemoglobin (oxygen-carrying molecules) and red blood cells in their blood, and had more microscopic liver damage than did unexposed dogs. These symptoms were observed at doses of 25 mg/kg per day in the rat study and 20 mg/kg per day in the dog study.[20]

A dog study which showed kidney effects at a tenfold lower dose (2.5 mg/kg per day) was originally used by EPA to calculate acceptable exposure to triclopyr.[21] However, this calculation was criticized by triclopyr's manufacturer because of studies the company conducted showing that triclopyr is more slowly excreted by dogs than other animals, and that the dog kidney is more susceptible than the kidney of other animals.[22,23] As a result, EPA classified the kidney damage as "not a toxic response to the test chemical, but a physiologic response of the dog"[24] and did not use the results in its more recent evaluation of triclopyr.[24]

There are no publicly available chronic toxicity studies of commercial triclopyr-containing products.

Mutagenicity

Triclopyr's mutagenicity (ability to cause genetic damage) has been studied in a variety of laboratory tests. One study looked at triclopyr's ability to cause dominant lethal mutations in rat embryos. Dominant lethal mutations are mutations in sperm that cause the death of the embryo fertilized by the defective sperm, and are studied by counting the number of dead embryos in pregnant animals. In a study of female rats mated with males who had been dosed with triclopyr, the frequency of embryo loss increased at the middle and high dose (7 and 70 mg/kg).[25]

In seven studies of other kinds of genetic damage that were submitted by triclopyr's manufacturer in support of its registration as a pesticide, no mutagenicity was observed.[25]

There are no publicly available mutagenicity studies of commercial triclopyr-containing products.

Carcinogenicity

Triclopyr's carcinogenicity (ability to cause cancer) has been studied in rats and mice. In both species, feeding of triclopyr significantly increased the frequency of breast cancer (mammary adenocarcinomas).[26]

In EPA's evaluation of these studies, the agency called this carcinogenic response "marginal."[26] EPA therefore classified triclopyr as a Group D carcinogen, one that is "not classifiable as to human carcinogenicity,"[26] even though EPA's guidelines call for classifying pesticides as carcinogens if they cause cancer in laboratory tests of more than one species.[27]

In male rats, triclopyr caused an increase in the frequency of adrenal tumors.[26]

There are no publicly available carcinogenicity studies of commercial triclopyr-containing products.

Effects on Reproduction

Triclopyr, its triethylamine salt, and its butoxyethyl ester have all caused reproductive problems in laboratory tests. Rats fed triclopyr for two generations had smaller litters and smaller offspring than did unexposed rats. Pregnant rats fed the amine salt had offspring that weighed less and had more skeletal abnormalities than offspring from unexposed rats. Pregnant rabbits fed the amine salt had fewer litters, fewer live fetuses, and more embryo loss than did unexposed rabbits. Pregnant rabbits fed the ester had fewer live fetuses, more embryo loss and offspring with more skeletal abnormalities than did unexposed rabbits. These reproductive problems occurred at doses of 100 and 250 mg/kg per day.[28]

Recently, pesticide regulators, researchers and the general public have become increasingly concerned about more subtle effects on reproduction. Of special concern has been the possibility that pesticides might interfere with the devel-

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Source: Pages 59-60 of this publication are drawn from Global Pesticide Campaigner, April 2001, Vol. 11, No. 1. Published by Pesticide Action Network-NA, San Francisco, USA

Imidacloprid

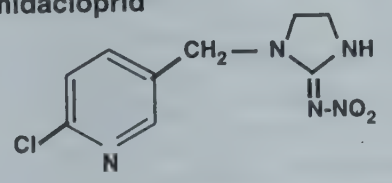
A factsheet by the Northwest Coalition for Alternatives to Pesticides (NCAP)

- Imidacloprid is a relatively new, systemic insecticide chemically related to the tobacco toxin nicotine. Like nicotine, it acts on the nervous system. Worldwide, it is considered to be one of the insecticides used in the largest volume.
- It has a wide diversity of uses: in agriculture, on turf, on pets and for household pests.
- Symptoms of exposure to imidacloprid include apathy, labored breathing, incoordination, emaciation and convulsions. Longer-term exposures cause reduced ability to gain weight and thyroid lesions.
- In studies of how imidacloprid affects reproduction, exposure of pregnant laboratory animals resulted in more frequent miscarriages and smaller offspring.
- An agricultural imidacloprid product increased the incidence of a kind of genetic damage called DNA adducts.
- Imidacloprid is acutely toxic to some bird species, including sparrows, quail, canaries and pigeons. Partridges have been poisoned and killed by agricultural use of imidacloprid. It has also caused eggshell thinning.
- The growth and size of shrimp are affected by imidacloprid concentrations of less than one part per billion (ppb). Shrimp and crustaceans are killed by concentration of less than 60 ppb.
- Imidacloprid is persistent. In a field test in Minnesota, the concentration of imidacloprid did not decrease for a year following treatment. It is also mobile in soil, so is considered by the U.S. Environmental Protection Agency to be a potential water contaminant.
- The development of resistance to imidacloprid by pest insects is a significant concern. In Michigan potato fields, the Colorado potato beetle developed resistance to imidacloprid after just two years of use.

By Caroline Cox

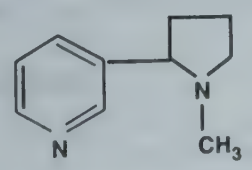
Imidacloprid (see Figure 1) is a relatively new insecticide, first registered for use as a pesticide in the U.S. in 1994, and was the first insecticide in its chemical class to be developed for commercial use.[1] Imidacloprid is a systemic insecticide[1]; it moves through plants from the place where it was applied and kills insects when they feed. Its major manufacturer is Bayer Corporation that markets imidacloprid products with the brand names Merit, Admire, Premise, Pre-Empt and Advantage, among others.[2-6]

Figure 1
Imidacloprid



1-((6-chloro-3-pyridinyl)methyl)-N-nitro-2-imidazolidinimine

Figure 2
Nicotine



Use

Although imidacloprid has not been in use for long relative to other common pesticides, according to University of Arizona entomologist George Ware "very possibly it is used in the greatest volume globally of all insecticides."[7] Imidacloprid has a wide variety of uses; it is used in agricultural products for use on cotton and vegetable crops,[3] in turfgrass and ornamental plant products,[2] in indoor and outdoor cockroach control products,[5] and in termite control products.[4] It is also used in products for pets, home, lawn and garden use including some, like potting soil, that may not always be easily recognized as pesticides.[6,8-10]

How does imidacloprid kill insects?

Imidacloprid and other insecticides in the nicotinoid chemical family are "similar to and modeled after the natural nicotine [a tobacco toxin]."[7] (See Figure 2.) Because of their molecular shape, size and charge, nicotine and nicotinoids fit into receptor molecules in the nervous system that normally receive the molecule acetylcholine. Acetylcholine carries nerve impulses from one nerve cell to another, or from a nerve cell to tissue that a nerve controls. Imidacloprid and other nicotinoids irreversibly block acetylcholine receptors.[7]

Why is imidacloprid less toxic to mammals' nervous systems than to insects'? Both insect and mammal nervous systems have acetylcholine receptors that are blocked by imidacloprid; most of the sensitive receptors are in the central nervous system of

Source: Pesticide Action Network-NA, San Francisco, USA

insects, but in nerves associated with muscles in mammals.[7] However, insect acetylcholine receptors are more sensitive to imidacloprid than are mammalian receptors,[11] although for some of imidacloprid's breakdown products this relationship is reversed.[12]

Inert ingredients

Commercial imidacloprid insecticides, like nearly all pesticides, contain ingredients other than imidacloprid called "inert" or "other" ingredients. There is little publicly available information about the identity of these ingredients. Inerts that have been identified in imidacloprid products include the following:

Crystalline quartz silica (in Merit 0.5 G[13]) is classified by the International Agency for Research on Cancer as "carcinogenic to humans"[14] and as "known to be a human carcinogen"[15] by the National Toxicology Program because it causes lung cancer. It also causes emphysema and obstructive airway disease and has also caused genetic damage in exposed people and laboratory tests.[15]

Naphthalene (in Leverage 2.7[16]) has recently been classified by the National Toxicology Program as having "clear evidence of carcinogenic activity"[17] (through inhalation exposure) because it causes nasal cancers. It also caused two kinds of chromosome damage in laboratory tests.[17] Other symptoms of naphthalene exposure include anemia, liver damage, cataracts and skin allergies.[18]

Whenever possible, the remaining sections of this article will specify whether tests were conducted with imidacloprid alone or with an imidacloprid-containing product (imidacloprid plus inerts).

Toxicity of inerts to cats: An unidentified inert ingredient in Advantage, an imidacloprid flea insecticide applied as drops on the back of a pet's neck, can be toxic to kittens when applied above the label rate. In laboratory tests, death, coma and incoordination were observed in kittens receiving five times the recommended dose of Advantage.[19] Further experiments showed that the toxicity was probably caused by the inert present in the largest amount.[20] No publicly available studies show the effects of smaller overdoses. Vomiting, salivation, and depression were also observed in cats fed Advantage or its inert ingredients.[21]

Acute toxicity

In laboratory animals, symptoms of acute (short-term) oral exposure to imidacloprid included apathy, labored breathing, loss of the abilities lasted for five days following exposure.[22]

Symptoms following acute exposure to an agricultural imidacloprid product (imidacloprid plus "inerts") included reduced activity, incoordination, tremors, diarrhea, and emaciation. Some symptoms lasted 12 days after exposure,[23] twice as long as the symptoms of exposure to imidacloprid alone. Symptoms following acute exposure to an imidacloprid flea control product included reduced activity, convulsions and labored breathing.[24]

Also in laboratory animals, symptoms of breathing imidacloprid (for four hours) included difficult breathing, loss of the ability to move, and slight tremors. Symptoms of breathing two agricultural imidacloprid products were similar: incoordination, convulsions, reduced activity, tremors and salivation. Some symptoms persisted two days after exposure.[25]

Eye irritation: Several imidacloprid products (Merit 0.5 G,[26] Merit 75 WP,[2] Premise 75,[4] Provado Solupak,[27] and Advantage[6]) cause eye irritation.

Worldwide, imidacloprid is considered to be one of the insecticides used in the largest volume.

Subchronic toxicity

Subchronic (medium-term; 10-day) exposure of rats to imidacloprid reduced weight gain at a dose of 10 mg/kg per day.[28]

There are no publicly available subchronic studies of commercial imidacloprid products.

Chronic toxicity

Chronic (long-term; lifetime) feeding studies with rats showed that the thyroid is especially sensitive to imidacloprid. Thyroid lesions were caused by doses of 17 milligrams per kilogram (mg/kg) of body weight per day in males. Slightly higher doses (25 mg/kg per day) reduced weight gain in females.[29] At higher doses (100 mg/kg per day), effects included atrophy of the retina in females.[30]

There are no publicly available chronic studies of commercial imidacloprid products.

Effects on reproduction

Imidacloprid affects reproduction in a variety of ways. In pregnant rabbits, imidacloprid fed between the sixth and eighteenth days of pregnancy caused an increase in the frequency of miscarriages and an increase in the number of offspring with abnormal skeletons. These effects were observed at a dose of 72 mg/kg per day. In rats, a two generation feeding study found that rats fed imidacloprid gave birth to smaller offspring. Their weight was reduced at a dose of 19 mg/kg per day.[31]

There are no publicly available studies of the effects of commercial imidacloprid products on reproduction.

Mutagenicity

The tests of imidacloprid's ability to cause genetic damage that were submitted to the U.S. Environmental Protection Agency (EPA) as part of the registration process found no evidence of genetic damage, or evidence only at high exposures.[1] However, a new technique that looks at the ability of a chemical to cause genetic damage by chemically binding to DNA (the genetic material) found that the imidacloprid insecticide Admire increased the frequency of this kind of damage. DNA adducts (the

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binding of a chemical to DNA) were five times more common in calf thymus cells exposed to Admire than in unexposed cells.[32]

Toxicity of imidacloprid's metabolites

Several of imidacloprid's breakdown products (metabolites) can be toxic. One metabolite found in imidacloprid-treated plants, called the olefine metabolite, is more toxic to insects than imidacloprid itself.[33] Another metabolite, the desnitro metabolite, has very little nervous system toxicity to insects[33] but is more toxic than imidacloprid itself in mammals' nervous systems.[12] The soil metabolite 2-imidazolidone[34] (also known as ethyleneurea) induces tumors in combination with nitrate[35] and causes genetic damage.[36]

Other problems caused by imidacloprid in birds include eggshell thinning, decreased weight and reduced egg production and hatching success.

Effects on birds

Imidacloprid's acute toxicity to birds varies widely among bird species. However, it is "highly toxic"[1] to certain species including house sparrow,[1] Japanese quail, canary and pigeon.[37] The median lethal dose (LD_{50}; dose that kills half of a test population) for all these species is less than 50 mg/kg.[1,37] Based on these tests, EPA's Ecological Effects Branch concluded that the agency's "levels of concern" were exceeded for both nonendangered and endangered songbirds.[38]

Imidacloprid causes abnormal behavior at doses less than 1/5 of that which causes death. House sparrows fed a granular imidacloprid product at doses of 6 mg/kg showed symptoms of incoordination, lack of responsiveness, and inability to fly. At doses of 12 mg/kg diarrhea and immobility were added to the observed symptoms.[39] Even birds for whom imidacloprid is not highly toxic, mallard ducks for example, show these symptoms. Symptoms were observed in mallards at all imidacloprid doses used in tests submitted to EPA as part of the registration process.[40]

Other problems caused by imidacloprid in birds include eggshell thinning (at exposures of 61 mg/kg),[1] decreased weight (at exposures of 150 ppm in food),[41] and reduced egg production and hatching success (at exposures of 234 ppm in food).[42] French veterinarians have found dead and poisoned partridges in agricultural fields following use of imidacloprid-treated seed and verified that the birds' symptoms matched those caused by imidacloprid. Imidacloprid residues were found in the crop, gizzard, and liver of these birds.[43]

Effects on fish

Imidacloprid is acutely toxic to adult fish at relatively high concentrations (over 80 ppm). Juvenile fish are considerably more susceptible. Survival of rainbow trout fry, as well as their weight, was reduced at the lowest imidacloprid concentration tested (1.2 ppm). Therefore it was not possible to determine the lowest concentration that did not cause adverse effects.[44]

Effects on other aquatic animals

Imidacloprid is toxic at extremely low concentrations to some species of aquatic animals. The following species have been studied as representatives of aquatic animals in general:

- The LC_{50} for the widespread freshwater crustacean *Hyalella azteca* is 55 ppb, classified by EPA as very highly toxic. Some mortality was recorded at a concentration of less than 1 ppb.[45]
- Imidacloprid's LC_{50} for the estuary crustacean *Mysidopsis bahia* is 37 ppb. Behavioral effects occurred in those animals that survived exposure: lethargy and loss of equilibrium.[46] The LC_{50} for an agricultural imidacloprid product was similar and EPA also classified it as very highly toxic.[47] Sublethal effects on mysid shrimp occurred at startling low concentrations: length, growth and production of offspring were all reduced at concentrations less than 1 ppb.[48] Mysid shrimp occupy "an important position in near shore food webs. They constitute a major source of food for many fish species...." In addition, "indirect effects to waterfowl may be expected if the mysid population, or similar organisms, is depleted."[49]
- A study of artificial ponds found that the number of invertebrate species and their abundance was reduced at concentrations of 5 ppb.[50]

Effects on earthworms

Earthworms are an important part of the soil ecosystem. In a typical soil, about 80 percent of the animals, by weight, are earthworms. They make important contributions to soil fertility and the breakdown of organic material.[51] Imidacloprid is acutely toxic to earthworms; for example, the LC_{50} of the species *Eisenia fetida* is between 2 and 4 ppm in soil.[51]

At lower concentrations, other effects occur. The activity of the enzyme cellulase, which is found in the earthworm's gut and allows it to break down plant litter, is reduced by imidacloprid concentrations of 0.2 ppm.[52] The frequency of deformed sperm in earthworms was increased by a soil concentration of 0.2 ppm. The frequency of damaged DNA (genetic material) in earthworms was increased by a concentration of 0.05 ppm.[51]

Effects on beneficial insects

Since imidacloprid is an insecticide, it is not surprising that it is toxic to beneficial insects, those that provide an economic benefit to agriculture. Examples include the following:

- Imidacloprid is highly toxic to honey bees.[1]
- Lab tests indicated that no adults and only 10% of juvenile spiny soldier bugs (a predator of potato beetle, corn earworm and other pests) would survive a typical application of imidacloprid.[53]
- Treatment of vegetable crops with the imidacloprid insecticide Provado reduced parasitoids of whiteflies between 35%–50%.[54]
- Treatment of marigolds (with the imidacloprid insecticide Admire) or honeylocust trees (with the imidacloprid insecticide

Merit) increased spider mite damage on both species because the insect natural enemies of the spider mites were killed by the imidacloprid.[55] A similar resurgence of spider mites occurred in eggplant treated with imidacloprid granules at planting.[56]

- Soil treatment of sunflowers, chrysanthemums and dandelions with imidacloprid granules (Marathon) caused a decrease in the ability of lady beetles (predators) on the plants to move.[57]
- An imidacloprid insecticide was acutely toxic to a variety of predatory insects in laboratory tests: mirid bugs, lady beetles (adult and larvae) and lacewings.[58]

Effects on cats

A British veterinarian reported that a cat (that was already ill with cancer) developed a severe skin rash following treatment with Advantage. The rash, centered at the spot where the imidacloprid was applied, caused intestinal problems and heart failure, leading to death.[59]

The development of resistance to imidacloprid in pest species appears to be a serious concern. In Michigan, imidacloprid resistance in the Colorado potato beetle was documented following two years of use on potatoes.

Effects on plants

Although it is perhaps surprising for an insecticide, imidacloprid can be toxic to plants. For example, lemon seedlings growing in a greenhouse were damaged by trunk treatments with an imidacloprid insecticide,[60] and cauliflower seedlings were damaged by root drench and soil treatments.[61] In addition, a Polish researcher reported that treatment of peas with the imidacloprid insecticide Gaucho increased the incidence of *Fusarium* root rot.[62]

Also, an imidacloprid insecticide decreased growth of blue-green algae and diatoms at moderate concentrations (9–33 ppm).[63,64]

Food contamination

Little monitoring of imidacloprid in food crops is publicly available. The U.S. Department of Agriculture and the Food and Drug Administration do not include imidacloprid in their food monitoring programs.[65,66] There are two published imidacloprid monitoring studies from Spain. One found imidacloprid residues in all samples of greenhouse vegetables tested one week after treatment.[67] The other found imidacloprid in tomatoes, peppers, potatoes, carrots, eggplant, pears, and melons; 21% of the samples were contaminated.[68]

Water contamination

Imidacloprid, according to EPA, "has the potential to leach to ground water. In addition, high solubility and mobility are concerns for transport to surface water by dissolved runoff."[69] Details about these concerns include the following:

- Persistence of imidacloprid varies among sites in tests submitted as part of its registrations, but is always significant. The shortest half-life (the amount of time required for half of an applied pesticide to break down or move away from the test site) was 107 days in turf-covered soil in Georgia. The longest half-life was in Minnesota where the imidacloprid concentration in cornfield soil did not decline for one year after treatment.[70]
- Imidacloprid's ability to move in soil[69] has been demonstrated by a variety of studies. In a laboratory test, imidacloprid leached more quickly through soil columns than the other 11 pesticides tested.[71] Some of the other pesticides included in this study, diazinon, chlorpyrifos and diuron, are widespread water contaminants.[72] EPA modeled the relative leaching potential of 14 turf insecticides; imidacloprid was in category I, pesticides with highest leaching potential.[73] When applied in a hop field drip irrigation system, imidacloprid moved to the maximum depth tested (105 cm) within seven days after application.[74] (This represents a high-leaching scenario, as the soil was irrigated daily, but is a good example of imidacloprid's mobility in soil.)

Despite the concern raised by these studies that imidacloprid will contaminate water, EPA did not classify it as a restricted use product in order to protect water quality.[75] EPA explained their actions this way: "We are not recommending that the turf and ornamental products be classified as restricted use products due to ground water concerns for several reasons. First, several of the proposed NTN products contain directions for use around the home and a Restricted Use Classification would not allow sale of these products to the homeowner. Second, professional lawn care companies will be users of these products and they will not use a Restricted Use Product."[76] Thus, the decision was an economic one, not a scientific one.

Resistance

The development of resistance to imidacloprid in pest species appears to be a serious concern. In Michigan, imidacloprid resistance in the Colorado potato beetle was documented following two years of imidacloprid use on potatoes. (In both years, over 80% of the potato acreage was treated with imidacloprid.)[77] In laboratory experiments, thrips selected for their resistance to the organophosphate insecticide diazinon were also resistant to imidacloprid.[78] This situation, in which resistance to one insecticide confers resistance to another insecticide, is called cross-resistance and is "especially disconcerting"[78] to the University of Missouri researchers who conducted the study.

Caroline Cox is editor of the Journal of Pesticide Reform *(JPR), a publication of the Northwest Coalition for Alternatives to Pesticides (NCAP).*

This information originally appeared in JPR 2001 Spring issue. To find out more about NCAP and the Journal of Pesticide Reform, *visit their Web site at http://www.pesticide.org. NCAP, P.O. Box 1393, Eugene,*

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Source: Pages 61-65 of this publication are drawn from Global Pesticide Campaigner, August 2001, Vol. 11, No. 2. Published by Pesticide Action Network-NA, San Francisco, USA

Atrazine

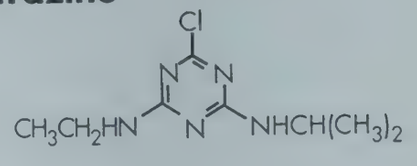
A factsheet by the Northwest Coalition for Alternatives to Pesticides (NCAP)

- Atrazine, a triazine herbicide, is one of the two most commonly used agricultural pesticides in the U.S.
- According to the National Toxicology Program, atrazine is "immunotoxic," disrupting the function of the immune system.
- Exposure to atrazine also disrupts hormone systems. Detailed research, much of it done by the U.S. Environmental Protection Agency (EPA), showed that testosterone, prolactin, progesterone, luteinizing hormone, estrogen and a thyroid hormone are all affected by atrazine.
- In laboratory tests, atrazine delays puberty. In addition, inflamed prostates occur more often in the offspring of mother animals that were fed atrazine while they were nursing than in the offspring of unexposed mothers.
- Atrazine is a pervasive water contaminant. It is the most common pesticide found in rivers, streams and groundwater. The U.S. Geological Survey's (USGS's) recent national monitoring study found atrazine in rivers and streams, as well as groundwater, in all 36 of the river basins that the agency studied. It is also often found in air and rain.
- In lakes and groundwater, atrazine and its breakdown products are persistent, and can persist for decades. It is also persistent in soils. Half lives (the amount of time required for 50% of the atrazine applied to disappear) can be over 100 days in surface layers of soils. Below the surface, atrazine can persist for years.

by Caroline Cox

Atrazine (see Figure 1) is a widely used herbicide in the triazine family. Certain crops (primarily corn and related crops) are tolerant of atrazine, and it is used to kill weeds without crop death in those situations.[1] Atrazine was first registered in the U.S. in 1959.[2] Currently, the major manufacturer is Syngenta (formerly Novartis Crop Protection, Inc.),[3] but it is marketed by many companies.[4] Use of atrazine has been the subject of significant concerns because it is one of the most commonly detected pesticide contaminants of rivers, streams and wells.[5]

Figure 1
Atrazine



2-chloro-4-ethylamino-6-isopropylamino-s-triazine

Use

Atrazine is "one of the two most widely used agricultural pesticides in the U.S."[6] according to the U.S. Environmental Protection Agency (EPA). Estimated annual use is between 64 and 75 million pounds. The primary crops on which atrazine is used are corn, sorghum and sugar cane.[7]

Mode of action

Atrazine kills plants by blocking photosynthesis, the process by which green plants use sunlight, carbon dioxide (from the atmosphere) and water to make sugars and related molecules. Without this "food," the plant is unable to grow and dies.[8]

Inert ingredients

Like most pesticide products, commercial atrazine products contain ingredients other than atrazine. Misleadingly called "inerts," the identity of most of these compounds is not publicly available.

Most of the toxicological tests used in the registration of a pesticide are done with the active ingredient only; when possible, the following summary of atrazine's toxicology will identify whether a particular study used atrazine alone or was done with commercial products (atrazine plus inerts).

Effects on the immune system

Four studies have shown that atrazine can disrupt normal immune system function, enhancing the risk of infectious disease or cancer.

In rats fed atrazine for three weeks, lymphopenia (a reduction in the number of white blood cells, cells that fight infection and disease[9]) was "pronounced"[10] at a dose of 100 mg/kg per day, the lowest dose tested.[11] This study compared immune system effects of 17 pesticides, and atrazine was one of five pesticides to which the immune system was most sensitive.[12]

In human blood cells, treatment with atrazine decreased the production of interleukin,[13] a regulatory protein in the immune system[14]; interferon,[15] an immune system protein that fights viral infections[16]; and tumor necrosis factor,[17] a protein that kills tumor cells.[18]

Cultures of spleen cells treated with atrazine produced fewer b-lymphocytes,[19] immune system cells that produce antibodies,[20] than untreated cells.[21]

A National Toxicology Program study of immune system function in mice concluded that "atrazine was found to adversely affect the immune system and, thus, is considered to be an immunotoxic compound."[22]

Source: Pesticide Action Network-NA, San Francisco, USA

Effects on hormones

The impact that environmental pollutants can have on the normal function of human and animal hormone systems has been a significant concern in the past decade.[23] Hormones are biologically active molecules that control growth, development, behavior and reproduction and thus are crucial to many important life functions.[24] Atrazine disrupts a stunning variety of hormone systems including the following:

- **Testosterone**. Often called the "male" sex hormone, testosterone promotes the development of male sex characteristics.[25] It is converted into biologically active forms in various organs. A series of studies showed that atrazine inhibits this conversion in male laboratory animals, reducing the amount of the active forms in the pituitary[26, 27] and the hypothalamus.[28] A single dose of 1 mg/kg was sufficient to cause this inhibition,[29] and the atrazine breakdown product deethylatrazine had similar effects.[30] In addition, the number of testosterone receptors in the prostate gland was reduced by atrazine exposure[31] in both young adult rats and older rats.[32] Atrazine also reduces the ability of an active form of testosterone to bind to receptor molecules in the prostate.[33] Atrazine exposure of mothers during pregnancy and nursing affects testosterone levels in their offspring: exposure during pregnancy increases the amount of the active form of testosterone in the pituitary of the female offspring, but exposure during both pregnancy and nursing reduces these levels in male offspring. In addition, exposure to either atrazine or deethylatrazine during nursing decreased the number of testosterone receptors in the prostate of male offspring.[34]
- **Prolactin**. Prolactin stimulates the production of breast milk in nursing females.[35] Atrazine inhibits "surges" of prolactin that occur during nursing and in response to release of estrogen ("female" sex hormones).[36, 37]
- **Progesterone**. Involved in the regulation of menstruation, progesterone also is important during pregnancy.[38] In female rats, exposure to atrazine induced "pseudopregnancies" in which, although the rats were not pregnant, their progesterone levels were high and the animals did not cycle through sexually active phases as they usually do.[39]
- **Luteinizing hormone**. Luteinizing hormone is produced in the pituitary gland and regulates the secretion of other sex hormones.[40] Atrazine blocks the "surge" of luteinizing hormone that occurs before ovulation.[41, 42]
- **Estrogens**. Often called "female" sex hormones, estrogens regulate the development of sex characteristics and the menstrual cycle, help maintain pregnancy and prepare the breasts for nursing.[43] Atrazine is not estrogenic; that is, it does not cause certain physiological activities that estrogens cause. Atrazine does not cause increases in uterus weight, as estrogens do, nor does it cause cell division that normally occurs in response to estrogens.[44] However, atrazine does have estrogen-related activities. It increases the activity of an enzyme called aromatase that converts testosterone and related hormones to estrogens, and thus could increase estrogen levels.[45] In a yeast that was genetically modified to produce the human estrogen receptor, atrazine displaced estrogens from the estrogen receptor at low estrogen concentrations, but not at high ones.[46] In addition, the atrazine breakdown product, deethylatrazine, has some estrogenic activity.[47]
- **Thyroid hormones**. In rats, atrazine caused a decrease in the blood levels of the thyroid hormone triiodothyronine,[48] a hormone that regulates metabolism and growth.

Studies of exposed people and laboratory tests show that atrazine and atrazine-containing herbicides reduce the ability to reproduce successfully.

Effects on reproduction

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Studies of exposed people have looked both at farmers and residents of agricultural areas. In the Ontario [Canada] Farm Family Health Study, the incidence of premature birth in families in which the father applied atrazine on the farm was nearly double that of families in which the father was not exposed to pesticides.[49] The incidence of premature birth was even higher in families where atrazine was used in the yard.[50]

Another study, conducted by the University of Iowa, studied communities whose drinking water came from an Iowa reservoir that was more contaminated with herbicides than other Iowa water supplies. The average atrazine contamination level in this reservoir was 2.2 parts per billion (ppb), just below the federal drinking water standard of 3 ppb. Elsewhere in the state levels averaged 0.6 ppb. Researchers found that the incidence of what is called intrauterine growth retardation (IUGR), babies with low birth weight for their gestational age, was about double the incidence of IUGR in towns with less contaminated water.[51] In a companion study, researchers found that the incidence of birth defects was more than double that in towns with less contaminated water. The incidence of limb reduction defects increased the most.[52]

A study that documented atrazine contamination of various tissues related to reproduction increases the concerns raised by the research summarized in the previous paragraphs. Researchers at the University of Bonn in Germany found atrazine in breast milk and cervical mucus in 20% (2/10) of the subjects tested.[53]

Effects on reproduction have also been demonstrated in female laboratory animals. Female rabbits which were fed atrazine had smaller litters and more miscarriages than unexposed rabbits. The lowest dose causing these effects was 75 mg/kg per day. In multigenerational studies with rats, animals fed atrazine had offspring which weighed less than the offspring of unexposed animals. The lowest dose causing these effects was 40 mg/kg per day.[54] At slightly higher doses (50 mg/kg per day), atrazine caused complete pregnancy loss (loss of the full litter) in rats of one laboratory strain (F344); similar results in other strains occurred at higher doses.[55]

Atrazine also disrupts the normal function of the male reproductive system in laboratory animals. In rats, atrazine caused a reduction in the ability of sperm to move and a reduction in the number of sperm in the epididymis, the part of the testes in which sperm mature. These effects were caused by a dose of 60 mg/kg given twice a week.[56]

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The atrazine breakdown product diaminochlorotriazine also reduces successful reproduction. Rats fed diaminochlorotriazine during pregnancy had offspring that weighed less than offspring of unexposed mothers and their bone development was also altered.[57]

Effects on development

Recent studies have shown that atrazine can affect juveniles as they develop into adults. In studies conducted by EPA scientists, sexual maturity is delayed in rats fed atrazine from the time they are weaned until puberty. In males a dose of 12.5 mg/kg delayed puberty while a higher dose (50 mg/kg per day) was required to cause a delay in females.[58, 59] In males, the primary breakdown products of atrazine have caused the same delay in puberty that atrazine does[60] as has exposure to atrazine before birth.[61]

Because feeding atrazine at relatively high doses reduces the weight of laboratory animals, it is possible that these effects on development could be related to reduced body weight rather than a direct effect of atrazine. To test this possibility, the EPA researchers in the studies of delayed puberty included in their experiments rats whose food was reduced so that their weight would match the weight of the atrazine-fed animals. In males, puberty was not delayed in the food-deprived animals as much as it was in the atrazine-fed animals.[62] Puberty of food-deprived females was not delayed.[63] Thus, atrazine directly affects the timing of puberty.

In addition, atrazine can affect the development of the prostate. When mother rats were treated with atrazine for the first four days after they gave birth (this is during the time that they are nursing their offspring), their male offspring were more likely to develop prostate inflammation. The dose required to cause inflammation was 25 mg/kg per day.[64] When pregnant rats were exposed to atrazine between the fifteenth and nineteenth day of their pregnancies, their male offspring also developed inflamed prostates.[65]

Mutagenicity

EPA recently evaluated tests of atrazine's mutagenicity, its ability to cause genetic damage. This review included tests submitted to the agency as part of the registration process and tests published in the scientific literature.[66] EPA concluded that "the available evidence did not indicate a mutagenic effect of atrazine exposure."[67]

However, the EPA review omitted studies that raise serious concerns about atrazine's mutagenicity. A 1998 study of chromosome damage in blood cells of workers in an atrazine production facility found that "occupational exposure to atrazine causes a significant increase in the percentage of chromosomal damage."[68]

Also omitted from the EPA analysis were studies that looked at the ability of atrazine to cause genetic damage at the concentrations at which atrazine has been measured in drinking water. The studies used cultures of cells from hamster ovaries, a standard cell culture for mutagenicity tests. The first study found that the incidence of chromosome breakage increased at concentrations less than 3 ppb,[69] the legally enforceable public drinking water standard.[70] A second study, using a similar protocol, found increased breakage of the largest chromosome at an atrazine concentration of 3 ppb (with borderline statistical significance) and a statistically significant increase at a concentration of 18 ppb. The highest atrazine concentration detected in Illinois water samples is 18 ppb.[71] The third study in this series found similar results: atrazine increased the frequency of chromosome damage at concentrations of both 3 and 18 ppb.[72] These studies measured a kind of genetic damage not studied in any research included in the EPA analysis.

A 1998 study of chromosome damage in blood cells of workers in an atrazine production facility found that "occupational exposure to atrazine causes a significant increase in the percentage of chromosomal damage."

The EPA analysis omitted consideration of the role that "inert" ingredients play in the mutagenicity of atrazine-containing herbicides. The tests submitted to EPA as part of the atrazine registration process are all tests using atrazine alone,[73] as are most of the published studies. NCAP has identified one study that compares a commercial atrazine product with atrazine alone. In this study, the commercial product caused about twice as many mutations as did atrazine.[74]

In addition, EPA failed to consider the implications of the atrazine derivative called N-nitrosoatrazine. N-nitrosoatrazine is formed in the human digestive system when both atrazine and nitrate are present.[75] Because both compounds are common water contaminants,[76] "there is much concern that this will increase the exposure to nitrosamines [N-nitrosoatrazine]."[77] Both atrazine and N-nitrosoatrazine can damage chromosomes in human blood cells. However, while concentrations of 1 part per million (ppm) of atrazine caused damage, much lower levels (0.1 ppb) of N-nitroso atrazine caused damage.[78] N-nitrosoatrazine was also "strongly mutagenic" in hamster cells.[79]

EPA also omitted consideration of synergistic effects with other herbicides. In a study in which human blood cells were exposed to low concentrations of linuron and atrazine (individually and together), both atrazine (at 1 ppb) and linuron (at 1 ppm) increased the frequency of broken chromosomes, but not significantly. The combination, at lower concentrations (0.5 ppm of linuron and 0.5 ppb of atrazine), caused a significant increase in broken chromosomes.[80] A study of chromosome breaks in the bone marrow cells of mice drinking water containing atrazine and/or the herbicide alachlor had similar results. Neither atrazine nor alachlor alone (at concentrations of 20 ppm) caused chromosome damage, but the combination (10 ppm of each) did.[81] Like atrazine, alachlor is a common water contaminant.[82]

Although tests on cells from humans or other mammals should be most relevant to human hazards, EPA has given little consideration to the type of organism used in the mutagenicity studies they evaluated. In the tests using bacteria and yeast, only a few (5/23) were positive (showed genetic damage). However, in the tests using cells from humans or rodents a much larger proportion (10/23) were

positive.[83] An older (1980) review for the European Community of a smaller number of studies also noted that the type of organism was important: most positive results in this review were in mammals and in whole-animal rather than cell culture tests.[84]

Finally, the differences between data provided to EPA by atrazine manufacturers and data available in the published scientific literature are striking. A review published by EPA in 1993 found that all of the eight studies submitted for registration purposes were negative, but 14 out of 39 published studies were positive.[85]

Supporting evidence for the mutagenicity of atrazine comes from a study of a protein called p53 in rats fed relatively low doses of atrazine (2.7 mg/kg per day). This protein plays a central role in "DNA repair and survival after DNA damage." (DNA is the molecule from which genetic material is made.) The percentage of blood cells containing the p53 protein increased dramatically (about 20-fold) in the animals that were fed atrazine.[86]

Atrazine was the most commonly detected pesticide in river basins from all three land uses studied (agricultural, urban, and mixed).

Carcinogenicity

Whether or not atrazine is carcinogenic (causes cancer) is a controversial subject that has been studied in both people and laboratory animals. Studies of exposed farmers and farmworkers that have demonstrated an association between atrazine exposure and cancer include the following:

- Researchers from the Italian National Cancer Institute studied the association between triazine use and ovarian cancer in women corn farmers. They found that women who applied triazines, or cultivated fields where triazines had been used, were more than twice as likely to have ovarian cancer as unexposed women.[87]
- Researchers from the University of Kentucky studied the association between the incidence of breast cancer in Kentucky and a composite measure of triazine exposure. (The index was based on well and drinking water contamination data, acreage of corn production, and estimates of triazine use.) The study found that breast cancer risk was higher (1.1 to 1.2-fold) in counties with medium and high levels of triazine exposure than it was in counties with low exposure.[88]
- The Cancer Registry of Central California looked at correlations between atrazine use in California (by county) and the incidence of six types of cancer. The study found that for Hispanic males, the incidence of leukemia was associated with the use of atrazine. For black men, the incidence of brain and testicular cancer was associated with the use of atrazine.[89]
- Researchers from the University of Prince Edward Island and the University of Guelph studied associations between atrazine contamination of wells and drinking water and the incidence of six types of cancer in Ontario, Canada. They found the incidence of stomach cancer in both males and females increased with increasing atrazine water contamination.[90]

Atrazine has caused cancer in the following laboratory studies:

- In the Sprague-Dawley strain of laboratory rats, atrazine caused breast tumors in females.[91]
- In the F344 strain of rats, atrazine caused breast tumors in males. In females, atrazine caused cancers of the uterus, leukemia, and lymphoma.[92] (Another study of F344 rats, submitted as part of atrazine's registration, found no increases in tumors or cancer.[93])

One final laboratory study is not a standard carcinogenicity study but rather a study of cancer-causing mechanisms. In this study, using cell cultures from rat intestines and human colons, atrazine caused cells to proliferate, to increase in number. Human cells were more sensitive to atrazine than rat cells. Proliferation of colon or intestinal cells is part of the development of colon or intestinal cancer.[94]

EPA's evaluation of these studies concluded that atrazine is "not likely to be carcinogenic in humans." With respect to the studies of exposed people, the agency stated that "there is no supporting evidence or a sound argument of biological plausibility that these cancers may result from exposure to atrazine. Also, the lack of confirming studies indicates that the human investigations by themselves do not make a strong case for an association between atrazine exposure and human cancer."[95]

With respect to the laboratory studies, EPA concluded, based on detailed studies, that "it is unlikely that atrazine's mode of cancer action in SD [Sprague-Dawley] rats is operative in humans." The agency believes that atrazine causes cancer in Sprague-Dawley rats by weakening surges of luteinizing hormone. This initiates the equivalent of menopause earlier than it occurs in unexposed rats. During "menopause" in the Sprague-Dawley rat, levels of the hormone estrogen are high, which causes breast tumors. In humans, menopause causes low levels of estrogen, so the Sprague-Dawley rat results are not relevant.[96]

EPA's analysis leaves a critical question unanswered: if the hormonal effects of atrazine that cause breast cancer in Sprague-Dawley rats do not occur in humans, what is the effect on humans of this compound which appears to cause such significant disruption of hormone systems? What experiments can answer this question? Before giving atrazine a "not likely" cancer classification, shouldn't EPA find out what the effects in humans are likely to be? The International Agency for Research on Cancer (IARC) evaluated essentially the same set of studies and concluded that "atrazine is not classifiable as to its carcinogenicity to humans,"[97] leaving the door open for further studies. NCAP believes that IARC's conclusion is more appropriate and more protective of human health than EPA's conclusion.

Synergy

Synergy occurs when the combination of two chemicals is more toxic than either chemical alone. In terms of acute toxicity, atrazine is synergistic with a common class of insecticides, the organophosphates. A study using fruit flies as a test animal found that atrazine was synergistic with the organophosphate insecticides parathion, diazinon, dyfonate and phorate.[98] A second study, using aquatic midges as a test animal, found that atrazine was synergistic with the organophosphates trichlorfon, malathion, chlorpyrifos and methyl parathion.[99]

An insecticide in another chemical family, carbofuran, was also synergistically toxic with atrazine to fruit flies.[100]

Atrazine can also act synergistically with respect to effects other than acute toxicity. Atrazine causes more genetic damage in combination with other herbicides than it does alone. Another example

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concerns dinitrotoluene, a chemical that is transformed in the intestine of laboratory animals into carcinogenic and mutagenic compounds. Exposure to atrazine increased the formation of these mutagenic molecules.[101]

Contamination of rivers and streams

Atrazine frequently contaminates rivers and streams, according to the U.S. Geological Survey's (USGS's) National Water-Quality Assessment Program (NAWQA) begun in 1991. USGS has compiled data from the first 20 river basins studied by NAWQA and the summary paints a startling picture of atrazine contamination.[102] Atrazine was the most commonly detected pesticide in river basins from all three land uses studied (agricultural, urban and mixed), and the atrazine breakdown product deethylatrazine was also commonly found. In agricultural basins, USGS found atrazine in about two-thirds of the samples tested. In urban basins, USGS found atrazine in 70% of the samples. In major rivers with mixed land uses, USGS found atrazine in 80% of the samples. Concentrations were as high as 120 parts per billion (ppb) in agricultural basins, 14 ppb in urban basins and 22 ppb in river basins with mixed land uses.[103] At both agricultural and mixed land use sites, concentrations were close to or exceeded the U.S. drinking water standard of 3 ppb in about 5% of the samples.[104]

For information about contamination of a particular river basin, the NAWQA Web site is an excellent resource: http://water.usgs.gov/pubs/nawqasum.

NAWQA and other studies document important patterns in atrazine's contamination of rivers and streams:

- Atrazine contamination is not geographically restricted. It is common in the midwestern "Corn Belt" where use is widespread, but rivers and streams from all 36 basins that have been studied by NAWQA are contaminated.[105] Contamination is common in locations as diverse as Oregon's Willamette Valley,[106] south-central Texas,[107] Denver, Colorado,[108] and New York's Hudson River.[109]
- Highest atrazine concentrations are found in rivers and streams when there is rain following spring atrazine applications to agricultural land. These pulses of atrazine can exceed the drinking water standard set by EPA and are not removed by conventional water treatment.[110] For example, the cities of Lincoln and Omaha, Nebraska, draw their water from wells that are "hydraulically connected" (located near and using the same water) to the Platte River at Louisville, Nebraska. USGS found atrazine above EPA's drinking water standard in one third of the samples of river water from Louisville.[111]
- However, atrazine is often found year round, although concentrations are lower than they are during the spring.[112, 113] Atrazine found during other seasons probably enters the river from contaminated groundwater. This contamination can originate at "some distance from the river."[114]
- Heavy rainfall and full streams lead to the highest pulse concentrations of atrazine, indicating that it is "a readily available constituent in the watershed that is being washed off in proportion to the amount of excess rainfall (runoff)."[115] Smaller rivers have larger and more abrupt pulses, while in large rivers, elevated concentrations can be spread out over several months.[116]
- There is not a simple relationship between atrazine use and levels found in rivers and streams. USGS scientists recently summarized atrazine loads in the Mississippi River between 1975 and 1997. While atrazine use in this basin declined during this period (from 38,000 to 25,000 tons), atrazine loads in the river did not decrease.[117] In smaller rivers and streams, however, and over a shorter time period (1989-1994), USGS found significant decreases in concentration even though use had declined only slightly. One possible explanation is that restrictions in atrazine use were implemented at this time.[118]
- Atrazine contamination of water is not restricted to areas downstream from where it is used. For example, British researchers who intensively studied a small watershed concluded that "atrazine was found at relatively high concentrations when it had not been applied to any of the fields draining to the sampling point."[119]

Contamination of groundwater

Atrazine commonly contaminates groundwater. It has been found in the groundwater of all 36 river basins studied by USGS.[120] Atrazine was often the most common pesticide detected. Deethylatrazine, formed when atrazine breaks down, was also common. About one-third of the agricultural well samples were contaminated with atrazine in the first 20 basins studied, as were about 15% of the urban samples and 10% of the samples from mixed use basins.[121]

Important reasons for atrazine's presence in ground water are its widespread use and long persistence.[122]

Reducing atrazine use can reduce groundwater contamination. For example, atrazine use in Iowa declined by 12% between the mid-1980s and the early 1990s. Over the same interval, the frequency of atrazine-contaminated wells declined 14%.[123]

As with rivers and streams, atrazine has contaminated groundwater in areas where it has not been used nearby. Researchers from Environment Canada studying prairie springs found atrazine when "it was not used anywhere in the vicinity of the aquifers."[124] They suggest that transport in the atmosphere is the most likely source.[125]

Contamination of rain

Atrazine is commonly found in rain. A USGS compilation of national, multistate, state and local monitoring studies showed that atrazine was found at nearly every site where rainfall was collected.[126] In some cases, concentrations in rain are above drinking water standards.[127] The amount of atrazine deposited in rain can be large. For example, USGS calculates that the rain deposits 110,000 kilograms of atrazine in the Mississippi River basin every year, over one-third as much as is carried annually by the river.[128] Rain also can be a significant source of atrazine in the ocean: University of South Carolina researchers calculated that a two or three day rainstorm deposited atrazine along the South Carolina coast equal to 10% of the amount deposited annually by rivers.[129] Rain can carry atrazine long distances; for example, atrazine is deposited in rain in the remote Isle Royale National Park in Lake Superior.[130] Atrazine has also been found in fog in California.[131]

Persistence in lakes and ponds

According to EPA, atrazine "should be somewhat persistent"[132] in lakes or other water bodies with still water. In fact "somewhat persistent" may be an understatement. For example, USGS scientists estimate that persistence in deep lakes "may exceed 10 years"[133] and calculated that breakdown of atrazine in Lake Superior is "very slow (about 1% per year)."[134] Swiss scientists came to similar conclusions after studying a group of lakes: a small amount of atrazine degraded during the summer, otherwise the only losses of atrazine were by flushing. In 1989, Switzerland instituted "drastic application restrictions" for atrazine, but the amount of atrazine in the lakes did not decrease through 1994.[135]

Persistence in ponds is less, but still significant. German researchers found, for example, that the atrazine concentration in experimental ponds in April was over half what it had been the previous September, immediately after addition of atrazine.[136]

Persistence in groundwater

Atrazine is persistent in groundwater. For example, in a laboratory study, the half life for atrazine in groundwater sediments was almost six years[137] and a two month study "did not show a significant decrease"[138] in atrazine concentrations. In Delaware, USGS researchers estimated that the atrazine breakdown product deethylatrazine persisted for 25 years.[139]

Source: Pages 66-71 of this publication are drawn from Global Pesticide Campaigner, December 2001, Vol. 11, No. 3. Published by Pesticide Action Network-NA, San Francisco, USA

Oryzalin

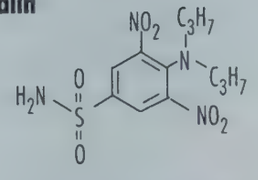
A factsheet by the Northwest Coalition for Alternatives to Pesticides (NCAP)

- Oryzalin is an herbicide used to control weeds in turf, in orchards and vineyards, around ornamental plants, and along rights of way. At least 2 million pounds of oryzalin are used annually in the U.S.
- Many oryzalin-containing herbicides cause eye irritation and also can cause skin allergies.
- In laboratory tests, oryzalin causes anemia. In addition, exposure of pregnant animals caused embryo loss, a reduction in the number of offspring in each litter, and a decrease in the weight of offspring. In a test of oryzalin's ability to cause cancer, exposed animals had more breast tumors, skin tumors, and thyroid tumors than unexposed animals. The U.S. Environmental Protection Agency (EPA) classifies oryzalin as a "possible human carcinogen."
- Oryzalin can persist in soil up to three years after application, and, according to EPA, is a "moderately mobile" herbicide in soil. Therefore it is not surprising that it often contaminates water. The U.S. Geological Survey found oryzalin in rivers, streams, or wells in almost half (16 of 36) of the river basins that the agency has tested nationwide.
- Animals can be adversely affected by oryzalin. Birds fed oryzalin gained weight more slowly than unexposed birds. It is also moderately toxic to freshwater fish, particularly juvenile fish, and is highly toxic to oysters.
- Oryzalin can have unexpected effects on plants that are not a target of the herbicide. For example, oryzalin increases the virulence of a rust that attacks flax plants. At concentrations that occur in soil after applications at typical rates, it decreases the growth of mycorrhizal fungi, beneficial fungi that grow in association with the roots of many plants.

by Caroline Cox

The herbicide oryzalin (see Figure 1), a member of the dinitroaniline chemical family, is commonly marketed under the brand name Surflan. It was first registered in the U.S. in 1974 and its primary manufacturer is DowAgrosciences LLC, formerly called Dow-Elanco.[1]

Figure 1
Oryzalin



3,5-dinitro-N4,N4-dipropylsulfanilamide

Use

Agricultural use of oryzalin, according to U.S. Environmental Protection Agency (EPA) estimates, is almost two million pounds per year. This includes use on turf (800,000 pounds per year), in almond orchards (350,000 pounds per year), and in vineyards (200,000 pounds per year). EPA believes that a "significant amount"[2] of oryzalin is also used around ornamental plants and along rights of way, but says that estimates of these uses are not readily available.[2] In addition, an estimated 1,800,000 applications are made annually around U.S. homes.[3]

How Does Oryzalin Kill Plants?

Oryzalin is a preemergence herbicide, meaning it kills seedlings as they germinate.[4] It kills young, growing plants by inhibiting the division of cells in the plant. Normally when cells divide, molecules of a protein called tubulin link together to form microtubules, long fiber-like structures that play critical roles in cell division. Oryzalin blocks the linking of tubulin, disrupting cell division.[5]

"Inert" Ingredients

Oryzalin products contain many ingredients other than oryzalin, and most of these, the so-called inert ingredients, are not identified on product labels.[6] Neither are they included in most of the toxicology tests required for registration.[7] For example, tests to determine whether oryzalin causes cancer, birth defects, other reproductive problems, and genetic damage have all been done just with oryzalin alone. For details about toxicological problems associated with some of the inert ingredients in oryzalin products, see "Hazards of Inert Ingredients," p. 25.

Source: Pesticide Action Network-NA, San Francisco, USA

All of the toxicology tests discussed in this article, with the exception of tests of eye irritation and skin allergies, were conducted on oryzalin alone.

Hazards to Eyes

Most oryzalin-containing herbicides cause eye irritation. NCAP surveyed labels from the 29 commercial oryzalin products whose labels are available on EPA's web site and found that 25 (over 85%) of them caused eye irritation.[8]

Skin Allergies

Most oryzalin-containing herbicides can cause the development of skin allergies in people who have prolonged or repeated exposures. In NCAP's survey of labels of oryzalin products, almost 80% had a warning statement about skin allergies.[8]

Medium- and Long-term Toxicity

Both three-month (subchronic) and two-year (chronic) feeding studies with rats and dogs found that oryzalin caused changes in blood similar to anemia. The number of red blood cells decreased; hematocrit (the proportion, by volume, of blood that is made up of red blood cells[9]) decreased; and the amount of the oxygen-carrying protein hemoglobin in the blood decreased. This anemia occurred at doses of approximately 50 milligrams per kilogram of body weight (mg/kg) per day.[10] Supporting evidence for this kind of effect comes from researchers at Central University in Venezuela who showed that oryzalin reduces the activity of enzymes involved in energy production in human red blood cells.[11]

Most oryzalin-containing herbicides can cause the development of skin allergies in people who have prolonged or repeated exposures.

Other adverse effects seen in chronic laboratory studies were increased weight of the liver and kidney as well as increased blood cholesterol levels.[10]

Effects on Reproduction

Oryzalin caused a variety of reproductive problems in laboratory tests.

The offspring of rats given oryzalin during pregnancy weighed less than the offspring of unexposed rats. Decreased growth also occurred in a study in which rats were fed oryzalin during three generations. These effects occurred at doses of 37.5 and 225 mg/kg per day.[12]

Rabbits given oryzalin during pregnancy had more embryo loss than unexposed rabbits and also had smaller litters. These effects occurred at a dose of 55 mg/kg per day.[12]

In addition, the uterus and ovaries of mice fed oryzalin for two years weighed less than these organs in unexposed mice. According to EPA, "As uterine weight is often under the influence of endocrine glands, one might suppose that oryzalin exerts a hormonal influence in these mice."[13]

Ability to cause cancer

EPA classifies oryzalin as a carcinogen (a chemical that causes cancer). The agency uses a "Group C" (possible human carcinogen) classification for oryzalin because three types of tumors (breast tumors, skin tumors, and thyroid tumors) occurred more frequently in a laboratory study of rats fed oryzalin than in unexposed animals.[14]

In 1994, EPA estimated the risk of cancer in people who apply oryzalin, assuming that applicators make one or 10 applications every year. The agency's calculations showed that users of most types of application equipment (low pressure handwand, backpack sprayer, and ground boom sprayer) exceeded EPA's acceptable risk for either the one- or 10-day exposure. However, EPA believes that requiring chemical resistant footwear (rubber boots), as the agency has done since 1995, "should adequately mitigate risk."[15]

Soil persistence

According to EPA, oryzalin often has a "biphasic" breakdown pattern in soil. This means that a portion of applied oryzalin breaks down relatively quickly, while the rest is more persistent. Oryzalin's half life (the amount of time required for one half of applied oryzalin to break down and move away from the application site) for the first breakdown phase in field studies is between 58 and 77 days. For the second phase it is between 138 and 146 days.[16]

Under some conditions, however, oryzalin can persist for much longer periods of time. On irrigated farmland in Idaho, oryzalin caused "extensive damage" to sugarbeets one year after treatment.[17] In Indiana, small amounts of oryzalin persisted for three years after application.[18]

Movement in Soil

Oryzalin is categorized by EPA as "moderately mobile" in soil. Interestingly, a researcher at an Israeli agricultural research institute found that surfactants, detergent-like molecules that are used in herbicides to help the herbicide move from the surface to the inside of the plant,[19] increase the mobility of oryzalin in the soil.[20] When combined with three common surfactants, oryzalin moved deeper into the soil than it did when it was applied alone. Oryzalin alone inhibited plant growth to a depth of 12 centimeters; with a surfactant this depth increased to 20 centimeters.[20]

Water Contamination

Given its persistence and mobility in soil, it's not surprising that oryzalin often moves into wells, rivers, and streams. The U.S. Geological Survey's (USGS's) national water monitoring program found that oryzalin contaminated rivers, streams, or wells in 16 of the 36 river basins studied by USGS.[21] Although there are no comprehensive data about which particular uses of oryzalin contaminate water, oryzalin has been found in runoff following applications of a granular oryzalin product to nursery containers,[22] and in ponds and wells on golf courses.[23,24]

Effects on Birds

While perhaps not expected for an herbicide, oryzalin can harm birds. A study in which oryzalin was fed to bobwhite quail showed that oryzalin reduced food consumption and body weight gain at

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all doses tested. EPA calculated that the amount of oryzalin that would be present on grass following a single application at the rate recommended for lawns and turf was greater than the lowest concentration of oryzalin causing the decreased weight gain (625 parts per million, ppm).[25]

Effects on fish

Oryzalin is classified as "moderately toxic" to fish because between 2 and 3 ppm are sufficient to kill fish. Juvenile fish are even more susceptible; less than 1 ppm caused adverse effects.[26]

Because of this toxicity the labels of all oryzalin-containing herbicides must include the warning statement, "This pesticide is toxic to fish. Do not apply this product directly to water, or to areas where surface water is present."[27]

The agency's [EPA's] calculations showed that applications at low rates (one pound per acre) could damage nontarget plants on adjacent areas

Effects on other aquatic animals

Oryzalin is classified by EPA as "highly toxic" to the Eastern oyster, one of the species used in pesticide testing to represent mollusk species that live in estuaries or the ocean. EPA's classification is based on a study showing that a concentration of less than 0.3 ppm is sufficient to reduce the growth of the oysters' shells.[28]

Another aquatic animal affected by oryzalin at low concentrations is the water flea, *Daphnia magna. Daphnia* is one of the species used in pesticide testing to represent fresh water invertebrates (insects, other arthropods, etc.). An oryzalin concentration of 0.6 ppm reduced the weight of *Daphnia* offspring.[29]

Effects on aquatic plants

Oryzalin is toxic to aquatic plants at extremely low concentrations. For example, 15 parts per billion (ppb) reduces the growth and reproduction of duckweed, one of the species EPA uses to represent aquatic plants in testing for ecological hazards.[30]

Effects on nontarget plants: Runoff and drift

Not surprisingly, small amounts of oryzalin are damaging to plants. For example, 2.2 ppb reduces root growth in oat seedlings.[31] This means that drift or runoff from fields or other areas treated with oryzalin can be sufficient to damage plants not intended as the target of the oryzalin application.

EPA estimated the amount of oryzalin in runoff assuming that just 1% of the oryzalin applied (by either aerial or ground applications) would be carried off by runoff and that the lowest application rate was used. The agency found that runoff under these conditions would be sufficient to damage nontarget plants on adjacent areas.[32]

For drift, EPA assumed that 5% of the amount of oryzalin used in an aerial application drifts onto adjacent areas. The agency's calculations showed that applications at low rates (one pound per acre) could damage nontarget plants on adjacent areas.[32]

Effects on Plant Diseases

Oryzalin may increase the susceptibility of some crop plants to diseases caused by fungi. In a study of a flax rust conducted at the Australian National University, a race of flax rust that is normally not able to attack flax grew and developed like a virulent race when the flax was treated with oryzalin. The researchers believe this was a result of oryzalin's ability to inhibit the formation of microtubules.[33]

Effects on Mycorrhizal Fungi

Mycorrhizal fungi are beneficial fungi that grow in association with many plant species and increase their growth and survival. Oryzalin reduces the growth of some of these fungi. Researchers at Auburn University (Alabama) tested eight species of mycorrhizal fungi associated with southern pines and found that oryzalin concentrations of 1 ppm reduced the growth of one species, and concentrations of 3 ppm reduced the growth of four species. While this study was done in a laboratory, these concentrations (1 and 3 ppm) are equal to concentrations found in soil after applications made at typical rates.[34]

Resistance

Weeds can develop resistance to oryzalin, the ability to survive exposure to this herbicide. Some populations of green foxtail, the most abundant weed of annual crops grown on Canada's prairies, can tolerate six times more oryzalin than normal plants. These populations are resistant to all herbicides in the dinitroaniline chemical family, as well as two other herbicides, dithiopyr and DCPA.[35] Goosegrass in cotton fields has also developed resistance to oryzalin and other dinitroaniline herbicides.[36]

Source: Pages 72-74 of this publication are drawn from Global Pesticide Campaigner, May 2002, Vol. 12, No. 1. Published by Pesticide Action Network-NA, San Francisco, USA

Lindane – a chemical of the past persists in the future

In recent months controversy has again focused on one of the oldest and insecticides still in widespread use. Lindane, which was only recently cleared by the UK authorities of a causative link with the blood disorder aplastic anaemia, has now been accused of increasing the incidence of breast cancer. We review the facts and figures about lindane and lay out the issues under debate.

What is lindane?

Lindane is an organochlorine insecticide which is still in relatively widespread use in developed nations as well as in the Third World. Many other organochlorines which have been linked to major health and environmental problems have been banned or receded from use. Included in this catalogue are aldrin, dieldrin and endrin. Others are DDT, heptachlor and toxaphene which have been banned in many countries but are still used quite extensively particularly in some developing countries.

Chemically, lindane contains at least 99% of the gamma-isomer of hexachlorocyclohexane (HCH). The organochlorines in general, and lindane in particular, are characterised by their broad spectrum insecticidal activity, long persistence in the environment, and their tendency to bio-accumulate along food chains.

While gamma-HCH and other isomers of HCH were isolated in the 19th century (lindane was first prepared by Faraday in 1825), its insecticidal properties were not recognised until the early 1940s; about the same time as DDT was developed.

The mode of action of lindane on insects is generally as a stomach poison with some fumigant action, i.e. it kills insects that ingest it or inhale its vapour. It kills insects by stimulating the central nervous system causing trembling, hyperexcitation, loss of coordination, paralysis, and eventually death. Although lindane acts on the nervous system of insects it is **not** a cholinesterase inhibitor as are the organophosphate insecticides, which were originally developed as nerve gases. The physiological mode of action of lindane is not well understood—it just works well as an insecticide.

Uses and usage

Lindane is currently approved for use in the UK as a wood preservative, agricultural and domestic insecticide. In all, 94 products containing lindane (or gamma-HCH as it is also known) are approved for use. It is approved for use against scabies and head lice. Veterinary uses of lindane in the UK ceased in 1991. The number of products containing lindane has decreased in recent years from over 400 in 1992. 100 products have had approval revoked but may continue in use until stocks have run out or their use is no longer permitted [1].

Lindane use in UK agriculture has increased since the 1980s, but may be showing some decline in more recent years. Table 1 shows its usage in various crop sectors. UK application is approved on cereals, oilseed rape, sugar beet, beans, brassicas, top fruit, cane fruit, field vegetables, protected vegetables and strawberries. It is also approved for use in forestry, on ornamentals and on turf, and is used as a seed treatment and in grain stores[3]. Non-agricultural approvals for lindane are mainly for timber treatments where its use has been steadily declining, and as a domestic insecticide to combat ants, moths, fleas and other insects. The approvals include products which are available for amateur use and several which may only be used by professionals.

Table 1 **Lindane usage in UK agriculture (ha)[2]**

Sector	Area treated/year		Area treated/year		Change
Arable crops	**732,430**	**1990**	**728,125**	**1992**	**-0.6%**
Grassland & fodder	**50,754**	**1989**	**51,613**	**1993**	**+1.7%**
Orchards	**1,552**	**1987**	**2,146**	**1992**	**+38.0%**
Protected crops	218	1981	265	1991	+21.5%

Toxic effects

As with any other pesticide active ingredient, toxicity trials carried out in laboratories reveal a range of acute and chronic health effects. Acute exposure mainly affects the central nervous system with manifested symptoms including vomiting and diarrhoea followed by convulsions. Exposure to small amounts by skin contamination or ingestion have been known to lead to headaches, nausea, dizziness, tremors and muscular weakness. Lindane is classified by the World Health Organization (WHO) as 'moderately hazardous' and has an oral LD_{50} in the rat of 88 mg/kg[4]. Human volunteers ingesting a dose of 17 mg/kg have experienced severe toxic symptoms, and a lethal dose to an adult would be in the region of 0.7-1.4 g [5].

Several cases of human poisoning by lindane have been reported. Children are significantly more susceptible to its toxic effects. In one case a dose equivalent to 62.5 mg/kg proved fatal, less than the LD_{50} of a rat. In adults, doses above 300 mg.kg ingested orally have proved fatal [6].

The reported chronic effects of exposure to lindane include nervous disorders and increased liver weight. It has not been found to be mutagenic but is embryotoxic. Trials to ascertain its carcinogenic potential have showed an increased incidence of benign and malignant liver tumours in mice when fed with doses of up to 600 mg/kg, but other animals did not produce such conclusive results [7]. The International Agency for Research on Cancer (IARC) has concluded that lindane is a possible human carcinogen (class 2B), and the US EPA has classified it similarly as a class B2/C possible human carcinogen.

Key health issues

Aplastic anaemia

Exposure to lindane has been linked with blood disorders known as blood dyscrasias, and in particular the disorder aplastic anaemia where the formation of platelets and white cells is disrupted. A great deal of work has been produced both proposing and refuting a possible link between blood dyscrasias and exposure to lindane. However, an extensive review carried out by the UK Advisory Committee on Pesticides (ACP)[8] has concluded that there is no conclusive link, but that in certain cases the development of the disease may be an idiosyncratic response to exposure to lindane. In many of the cases where patients who developed blood dyscrasias were exposed to lindane, they were also exposed to other pesticides. The ACP therefore says that lindane cannot be directly held responsible for causing the illness. The International Programme on Chemical Safety (IPCS) does not carry out an extensive review of the literature but reports that a number of cases of childhood aplastic anaemia were reputed to have been caused by lindane[9].

CHARGE

This condition which involves multiple congenital abnormalities has been linked to exposure of the mothers of CHARGE children to lindane during early pregnancy. A statistically significant proportion of mothers of CHARGE children in the UK were exposed to pesticides in early pregnancy, and one of the most prominent pesticides implicated was lindane[10].

This issue was addressed by the Health and Safety Executive (HSE)[11] and in a parliamentary debate[12]. HSE concluded that since mothers of CHARGE children were exposed to other chemicals in addition to lindane, no direct link can be proven. In the parliamentary debate, no response was given by the government.

Breast cancer

Lindane is an endocrine disruptor which is capable of imitating certain hormones in humans and thereby disrupting the physiological functions which these hormones control. There is a significant body of evidence which suggests that where lindane is used extensively, and particularly where cattle are exposed to it, the incidence of breast cancer is higher. The UK has the highest rate of death

Regulatory status

Lindane is banned for all uses in:

Belize *1985*
Ecuador *1985*
Finland *1988**
Hungary *1968*
Indonesia *1985**
Japan *1971*
Kuwait *1980**
New Zealand *1990**
Netherlands *1981*
Republic of Korea *1986*
St. Lucia*
Singapore *1984*
Sweden *1988**
Former Soviet Union *1988*

Lindane is severely restricted in:

Argentina *1972* Prohibited for use as an anti-weevil agent on seeds and products intended for human consumption.

Australia *1987* Only for control of white grub in pineapple.*

Austria *1992* Only for seed treatments.*

Bulgaria

China *1982* Prohibited for use on fruit trees, vegetables, herbs, tea, tobacco, coffee, pepper.

Colombia *1991* Certain formulation types banned.*

Cyprus *1987* Only permitted for timber treatment at <20% lindane.*

Dominica *1986*

Fiji Only licensed industrial users.*

Germany *1980* Prohibited for use on lactating cattle. Anti-fouling paints containing lindane cannot be used unless approval is granted by the appropriate authority.

Israel *1982* Approved for agricultural use only against locusts. Use revoked against scabies, pediculosis and in household sprays.

Morocco *1984* Only permitted as seed treatment.*

Philippines *1983* Prohibited for import except for emergencies as determined by the relevant authorities.

Poland *1987* Gradually withdrawn from agricultural and sanitary hygiene use.

Sri Lanka *1986* Only in coconut nurseries, locust control and medicinal uses.*

Yugoslavia *1972* Agricultural ban.

Lindane has specific uses restricted in:

Canada *1987* Data supporting some uses was inadequate and technical advances made some uses obsolete.

EC Countries *1988* Lindane (gamma-HCH) containing more than 1% of the other HCH isomers (alpha, beta, delta-HCH) is prohibited. Restricted for treatment of ground or seeds against soil insects.

Mexico *1978* Restricted agricultural use for rice, barley, maize and wheat.

US *1985* Vaporizers and smoke fumigation devices banned, and other uses must include label statements

Venezuela *1983* For use only: against disease vectors by the Ministry of Health; in agricultural pest emergencies; against ants and termites.

*Source: *Reference 21, others reference 22.*

from breast cancer in the world, and in Lincolnshire where lindane is used extensively on sugar beet crops, the rate of breast cancer is 40% higher than the national average[13].

The UK government has announced a breast screening programme with the aim of reducing the high rate of mortality from breast cancer. However, the government does not accept that lindane is responsible for causing breast cancer[14].

The presence of lindane in human milk has been reported in countries throughout the world[15]. Lindane residues are similarly detectable in cows milk and it is therefore clear that children, who have already been described as being more susceptible to the toxic effects of lindane, are ingesting the chemical from birth.

Environmental effects

Lindane is highly volatile, and when applied to field crops in particular, a high proportion (up to 90%) of the pesticide enters the atmosphere and is later deposited by rain. Concentrations of 5.5µg/l were detected in rain in Oxfordshire in 1992[16]. Lindane is also leached into surface waters and even into ground water. It has been found in increasing concentrations in the marine environment, and particularly in the North Sea [17].

The International Conference on the Protection of the North Sea agreed to reduce emissions from land, rivers and the atmosphere of a number of toxic chemicals including lindane by 50% between 1985 and 1995. Implementation of this agreement in the UK is in the form of a 'Red List' which includes lindane (gamma-HCH). A recent report suggests that the UK may not meet its reduction targets, and that in fact emissions of lindane to the North Sea from the UK increased by up to 50% between 1990 and 1991[18]. New figures published by the National Rivers Authority (NRA) show that total discharges of lindane from rivers to the North Sea increased between 1992 and 1993[19]. Lindane has also been detected in the North Pacific, Persian Gulf, Arabian Sea, Red Sea, Western Pacific, Indian Ocean, Antarctic Ocean and Arctic Ocean [20].

In common with other organochlorine pesticides lindane is fat soluble and this contributes to its tendency to bioaccumulate through food chains. Residues have been detected in the kidneys, livers and adipose tissue of a wide variety of wild animals and birds. It is highly toxic to aquatic invertebrates and fish.

Conclusions

Lindane has been in use long enough for a significant body of evidence on its toxic and environmental hazards to have built up. It has caused deaths and poisonings in humans and there is authoritative recognition of its long term health effects including carcinogenicity. It is a serious environmental contaminant and as well as being directly toxic to wildlife it bioaccumulates along food chains. A significant body of scientific and anecdotal evidence links lindane with serious health problems including aplastic anaemia, the birth disorder CHARGE and breast cancer.

Lindane has been banned or severely restricted in 37 countries and the ACP has so far carried out two reviews of lindane and continued to recommend its approval. The Pesticides Trust believes that lindane should be withdrawn from the market on the basis of existing evidence and as a precaution to avoid further health and environmental problems. Users seeking the least hazardous control option—as they are obliged to in the UK under COSHH regulations—should avoid the use of lindane entirely since safer alternatives are invariably available. (MD)

Dichlorvos (DDVP) – a hazardous organophosphate

Dichlorvos is an organophosphate (OP) insecticide widely used in developing countries. Because of its high acute toxicity and the consequent dangers to workers, there are concerns whether safe use is possible under such conditions.

Description

Dichlorvos is an insecticide of the organophosphate (OP) group. It has been in use since about 1955 and is used in the UK both professionally and in homes and gardens in a number of areas:

- in agriculture and horticulture it is used: in mushroom houses against mushroom flies; against various insects and beetles in poultry houses; and on protected ornamentals, protected vegetables and herbs and brassica seedlings;
- as a veterinary medicine, in protecting farmed salmon against salmon lice; and as an aerosol against cat and dog fleas;
- in public hygiene as an aerosol insecticide and space spray.

It also has wide uses in some developing countries as an insecticide on vegetables, deciduous fruits, rice and plantation crops such as cotton, coffee, tea, cacao, banana, tobacco and spices.

Dichlorvos is an insecticide with contact, respiratory and stomach action. Like many OP insecticides it also inhibits the enzyme cholinesterase, which results in disruption to the nervous and muscular system.

Regulatory status

In the UK, the non-agricultural uses of dichlorvos as an amateur and professional insecticide were reviewed by Health and Safety Executive in February (HSE) 1995[1]. Agricultural uses together with environmental effects will be included in a later review by the Ministry of Agriculture.

On a world-wide basis no country has banned dichlorvos, although there are restrictions in Indonesia, South Korea and Vietnam. Two recent international reviews of dichlorvos have been carried out: World Health Organisation (WHO) in 1989[2]; the Joint Meeting on Pesticides Residues (part of the UN Codex process) in 1994.[3]

Health issues

Acute toxicology

Dichlorvos has a high acute toxicity: the oral LD_{50} in rats is between 56 and 108mg/kg. It is classified by the WHO as a Class IB, 'highly hazardous'[4]. The dermal toxicity is similar to oral toxicity, and dermal exposure is a cause for concern.

Most human poisonings have resulted from the splashing of concentrated formulations onto the skin. Failure to remove the splash has proved fatal. Prompt removal has resulted in symptoms of intoxication but full recovery after treatment. Dichlorvos vaporises quickly. Cholinesterase inhibition has been reported from exposure by inhalation after the use of dichlorvos in non-ventilated or poorly ventilated areas[5].

Reports from the UK National Poisons Unit (NPU) show that between 1983 and 1990, 98 individual cases of poisoning involving dichlorvos were reported.

Dichlorvos is classified as 'toxic if swallowed', 'very toxic by inhalation', and 'toxic in contact with skin', by the NPU.

Chronic toxicity

Reproductive effects

The HSE review found: "No fertility studies which are both adequately conducted and reported... Individually no study is considered adequate to assess the teratogenic potential of dichlorvos in any species". In spite of these data gaps, government ministers ruled that: "Overall the weight of evidence indicates that dichlorvos does not present a risk to fertility and reproduction in humans."[6]

Neurotoxicity

There is evidence that dichlorvos can induce delayed neuropathy in hens at very high doses; and neurophysiological and behavioural changes in rats. But the HSE decided: "The significance of these findings for the risk assessment of dichlorvos is uncertain."[7]

Carcinogenicity

The International Agency for Research on Cancer[8] places dichlorvos in Group 2B (possibly carcinogenic to humans) based on what it considers to be sufficient evidence in animals, but inadequate evidence in humans. The US Environmental Protection Agency classifies it in category 2B (possibly carcinogenic to humans) but the result of further testing is awaited and it may be reclassified. The UK ACP, following its review in respect of non-agricultural uses, takes the view that "Overall, the weight of evidence presented does not suggest that dichlorvos is a carcinogenic risk for humans."

Genotoxicity

There is evidence that dichlorvos is mutagenic in bacteria, fungi, and mammalian cells *in vitro*, but that there is no evidence for mutagenicity in whole animals, when it is rapidly degraded.

Environmental effects

Dichlorvos is toxic to fish and aquatic arthropods are more sensitive than fish. It is highly toxic to birds and to honey bees.

Environmental Quality Standards have been proposed for the protection of UK freshwater and marine aquatic life. In setting the standards for dichlorvos, the Department of the Environment noted that "insufficient environmental data are available to verify the proposed standards for the protection of aquatic life."[9] However, by applying an arbitrary safety factor of 100 to the toxic dose for the most sensitive species, the Water Research Centre has recommended an annual average level of 0.001 µg/l (parts per billion) for freshwater species, and 0.04 µg/l for marine life in saline waters.

As a result of the Second North Sea Conference in 1987, a number of countries agreed to reduce discharges of certain chemicals to water. Dichlorvos is included in this UK Red List substances whose discharge is dangerous to water—and the UK government has agreed to reduce the discharge of such chemicals by 50% of their 1985 level by 1995. It is unlikely that this target will be met, as the main source of dichlorvos in water is from salmon farming which is an industry that has expanded greatly in recent years.

Food residues

Because dichlorvos degrades fairly rapidly it is not generally found as a residue on food. The UK Working Party on Pesticide Residues monitors residues in food, and dichlorvos is rarely found if at all.

Concerns

Salmon farming

Dichlorvos is licensed as a veterinary medicine by the Veterinary Medicines Directorate for use against sea lice (Lepeophteirus salmonis and Caligus elongatus) that afflict salmon. The UK salmon farming industry is mainly based in the western coast and Islands of Scotland there are about 130 salmon farming companies on 280 sites. Production has increased from 600 tonnes in 1980 to 48,000 tonnes in 1993[10]. There have been concerns about the discharge of dichlorvos as a result, and the possible effects of dichlorvos on wild salmon. There was an increase in the incidence of cataracts and blindness in wild salmon in the 1980s and this has been linked with exposure to dichlorvos[11].

Alternatives to dichlorvos are now being introduced including the use of sea wrasse as 'cleaner fish', and the use of hydrogen peroxide as an alternative disinfectant.

Developing country use

Because of its high acute oral and dermal toxicity, its availability in developing countries is a cause for concern. The Food and Agriculture Organisation (FAO), the World Bank, GTZ (Germany) and ODA (UK) generally discourage the procurement of such products. The accepted international guide to best practice in the procurement of pesticides is set out in the FAO's Provisional Guidelines on Tender Procedures for the Procurement of Pesticides[10] which state:

"Pesticide formulations that fall into Class IA or IB ... usually have severe restrictions in developed countries; in general they can only be used by specially trained and certi-

fied applicators. Such pesticides should not be used by small farmers or untrained and unprotected workers in developing countries"

Nevertheless research by the Pesticides Trust shows that dichlorvos is widely used in a number of countries where the conditions of use have raised concerns. Dichlorvos has caused poisonings in China, Costa Rica, Paraguay, India, Papua New Guinea and Egypt. It is also widely produced—there are facilities in India, Brazil and Mexico[13]. For these reasons PAN groups have strongly urged that dichlorvos be included in the Prior Informed Consent (PIC) process from the outset[14]. One manufacturer, Ciba Geigy, has agreed to withdraw dichlorvos from sale in the Colombian flower industry (see p14).

Conclusions

It is accepted that dichlorvos is dangerous to a number of aquatic species and that the discharge of dichlorvos to water should be reduced. Dichlorvos can inhibit cholinesterase levels in humans which may lead to short or longer term neurotoxic effects. Although it has been used for some 40 years, considerable uncertainties remain about whether or not it is implicated in cancer, and the wider environmental consequences of its use. In general and specifically in developing countries and in UK fish farming less hazardous alternatives are available. *(PB)*

Cypermethrin – a synthetic pyrethroid

Cypermethrin has become one of the most important insecticides in wide-scale use. It has been said that "no pesticide is perfect, but the pyrethroids come close."[1] Is this assessment accurate?

Description

Cypermethrin acts as a stomach and contact insecticide. It has wide uses in cotton, cereals, vegetables and fruit, for food storage, in public health and in animal husbandry. Its structure is based on pyrethrum, a natural insecticide which is contained in chrysanthemum flowers, but it has a higher biological activity and is more stable than its natural model. It was synthesised in 1974 and first marketed in 1977, by Shell (which has since sold their pesticide business to American Cyanamid.

In 1988, pyrethroids amounted to 40% of the sales for insecticides for cotton treatment in the world (cypermethrin 8%)[2], and cypermethrin is one of the most important insecticides for cereals and vegetables in the UK. There has been a dramatic increase in the use of cypermethrin for arable crops in the UK: from approximately 216,000 ha in 1988 to 1,582,000 ha sprayed in 1992, falling back to 863,000 ha in 1994[3]. It is also used for impregnation of mosquito bed nets to prevent malaria, and extensively for indoor pests. As many patents for pyrethroids expire between 1993 and 1996, the market looks set to open up dramatically[4].

Health issues

Acute toxicity

Cypermethrin is classified by the World Health Organisation (WHO) as 'moderately hazardous' (Class II)[5]. It interacts with the sodium channels in nerve cells through which sodium enters the cell in order to transmit a nerve signal. These channels can remain open for up to seconds, compared to the normal period of a few milliseconds, after a signal has been transmitted. Cypermethrin also interferes with other receptors in the nervous system. The effect is that of long-lasting trains of repetitive impulses in sense organs.

Symptoms of poisoning include abnormal facial sensations, dizziness, headache, nausea, anorexia and fatigue, vomiting and increased stomach secretion. Cypermethrin is also a skin and eye irritant. Normally, symptoms should disappear after some days but severely exposed patients additionally may suffer from muscular twitching, comata and convulsive attacks. In such cases, symptoms may persist for some weeks.

Most cases of pyrethroid poisoning have been reported in China[6] (nearly 600 between 1983 and 1988, of which 45 involved cypermethrin). They occur among farmers, mostly after misuse. Recently, poisonings have as well been reported after indoor use of pyrethroids in Germany among pest controllers and private users (see PN 29 p.3).

Chronic toxicity

Chronic symptoms after exposure to pyrethroids have now been reported[7]. Symptoms include brain and locomotory disorders, polyneuropathy and immuno-suppression, and resemble the multiple chemical sensitivity syndrome (MCS).

Carcinogenicity

Opinions differ as to whether cypermethrin is a carcinogen or not. Cypermethrin is classified by the US EPA as a weak category C oncogen—a possible human carcinogen with limited evidence of carcinogenicity in animals but no evidence of carcinogenicity in humans: it produced benign lung adenomas (tumours) at the highest dose level in female mice and has potential for liver carcinogenicity in rodents. However, the view of WHO is that as there was no evidence of carcinogenicity in male mice and as the results of mutagenic studies have been mainly negative "it is concluded that there is no evidence for the carcinogenic potential of cypermethrin."[8]

Mutagenicity

Cypermethrin was found to be genotoxic in mouse spleen and bone marrow[9] but other tests have been negative.

Immune suppression

Testing on rats has suggested that pyrethroids in general may have an immunosuppressive effect. WHO concludes that "more attention should be paid to this aspect, but at present, no opinion can be given about its relevance in the extrapolation of these data for man."[10]

Reproductive toxicity

When administered to pregnant and nursing rats, cypermethrin may lead to a functional delay in the brain maturation of the pups. The toxicity to young rats is higher the younger they are, also because the pathway for degrading cypermethrin is not readily developed in young rats.

Environmental effects

The pyrethroids are widely used because of their general low toxicity to birds and mammals. However, they are highly toxic to aquatic organisms and fish as well as to bees—with the same mode of action in each organism. The LC_{50} values for small fish and other aquatic organisms typically lie below 1 µg/l, and the LD_{50} value for bees is 0.03—0.12 µg/bee. For use with conventional hydraulic sprayers, buffer zones of 16-24 m are needed to reduce mortality of butterflies in the surroundings[11].

Although the direct acute toxicity towards birds is small, they are affected via the food chain: in a treated wood, only 20% of the nestlings of the blue tit, a beneficial bird, survived[12]. Other beneficial organisms that can be affected by cypermethrin include beetles, spiders and centipedes living on the soil and predatory mites. Populations are reduced to 20% in some experiments, but recover after some weeks.

Despite earlier findings, the microbial population of soil is affected by cypermethrin: the ammonification and nitrification in treated soils is enhanced, a sign of the environmental impact of cypermethrin[13]

Once applied, cypermethrin is bound strongly by soil components and is therefore not likely to enter ground water. Cypermethrin is not persistent in soil and quickly degrades to less toxic products (with a half life of 2 to 4 weeks). In contrast, cypermethrin persists in treated wood for up to seven months in the soil and on bark[14].

Residues

The relatively rapid degradation of cypermethrin means that it is not generally found as a residue in food. Residues have been found in UK imported lettuce, where one sample out of 30 exceeded the UK MRL[15], and in Pakistan, where the maximum residue level (MRL) was exceeded about 30 fold in turnip and okra (see PN p.19).

After indoor use, cypermethrin residues may be found in dust and carpets with a concentration up to 4 mg/kg[16]. The concentration in the air after an indoor treatment increases rapidly, but can then stay relatively constant for months at values for which pyrethroids can cause adverse health effects (3-8 µg/m^3) [17,18].

Recommendations for use

Safety precautions for handling include: avoid contact with skin and eyes; use PVC gloves, goggles, respirator mask, protective overalls and footwear; and keep children and pets away from areas being treated. In case of accidents, the following rules apply:

skin contact: remove contaminated clothes wash exposed areas with plenty of mild soap and water

eye contact: flush with clean water for 15 min. Seek medical aid

inhalation: keep subject under observation

ingestion: when the patient is conscious, provoke vomiting (by pharyngeal stimulation). Seek medical aid

Following investigations of a great number of poisonings in China, F. He gives the following recommendations for the use of pyrethroids[19]:

"Workers with skin diseases, central and peripheral nervous diseases should not be exposed to pyrethroids.

"Appearance of abnormal facial sensations during pyrethroid exposure indicates the necessity of reducing exposure (improved work practices, enhanced personal protection, improvement of ventilation, etc.).

"Exposure to pyrethroids should be ceased if the exposed subjects, in addition to having abnormal facial sensations, develop systemic symptoms such as headache, dizziness, nausea and fatigue. These subjects should not be allowed for readmission to work with pyrethroid exposure until all above-mentioned symptoms have disappeared."

Synthetic pyrethroids

Resistance

As the pyrethroids are chemically relatively similar, a pest species resistant to one member of the pyrethroid family is often resistant to another or even to all types[20]. Replacing one pyrethroid by another may not therefore be appropriate when resistance occurs. Resistance against cypermethrin is reported widely for the tobacco budworm (one of the most important pests on many crops in the US and Mexico)[21]. Some *Heliothis* species, the most serious pests on cotton, also developed resistance against pyrethroids, which led to severe yield losses worldwide[22]. The onset of resistance is frequently accompanied by increased doses of toxic pesticides, gradual loss of pest control and consequent loss of famers' income and increase in pesticide hazard.

Possible effects on the reproductive system

One report on an epidemic of gynecomastia (enlargement of the breast among males) among Haitian refugees[23] considers exposure to the synthetic pyrethroid phenothrin may be the cause. Experimental evidence suggests the pyrethroid molecule may bind to sex hormone binding globulin (SHBG) *in vitro*. Chronic exposure to pyrethroids may result in disturbances in hormonal effects relating to androgen action. Pyrethrins and in particular bioallethrin interact strongly with SHBG at concentrations of 40 mg/kg. The authors advise protection "from any form of contact or ingestion of the pyrethroids in order to prevent any undesirable effects on the human reproductive system until additional toxicological and endocrine studies can be conducted *in vivo*."

Cancer

A new study links leukaemia and lymphoid cancer with pyrethroid insecticides—although they showed only very little carcinogenic activity in previous toxicological studies. More than 20% of the leukaemia cases (women) and 10% (men) are linked with pyrethroid exposures (see PN28 p.27).

Problems with IPM

Synthetic pyrethroids will control a wide range of insects in a wide range of crops. Unfortunately, this broad-spectrum nature can adversely affect many non-target beneficials, distrupting, in particular, integrated pest management (IPM) programmes[24].

Indoor use

Recent research from Germany drew attention to potential health hazards of the use of synthetic pyrethroids in the home (see PN29 p. 3). There are also concerns raised by research about the development of resistance in indoor pest control[25].

In a petition of May this year (Drucksache 13/1478, 23 May 1995) the parliamentary group of the German SPD called upon the Federal Government to prohibit the use of pyrethroids in textiles and the interior and, in addition, to give advice on non-toxic methods of fighting pests.

Conclusions

New studies show that the health effects of cypermethrin and pyrethroids in general may be more severe than previous toxicological evaluations suggest. Further studies on carcinogenicity and chronic toxicity are required.

Carbaryl re-assessed

Carbaryl is widely used as an insecticide with acute toxic effects which are well known. Recent data on its carcinogenic potential has indicated the need for further research, and has prompted a revision of safety controls governing its use.

Description

Carbaryl, a carbamate insecticide, is a cholinesterase inhibitor, and can also act as a plant growth regulator. It is used to kill a range of chewing and sucking insects on over 120 agricultural crops. In UK agriculture, it is mostly used against caterpillar pests on apples. Internationally it is used on citrus fruit, mangoes, bananas, strawberries, nuts, vines, olives, okra, cucurbits, peanuts, soya beans, cotton, rice, tobacco, cereals, beet, maize, sorghum, alfalfa, potatoes, ornamentals and forestry. Carbaryl has also been used against earthworms in turf and amenity grass. Carbaryl is used against ectoparasites of humans and animals, including against head lice on children[1,2].

Carbaryl was introduced by Union Carbide (whose pesticide interests were taken over by Rhône-Poulenc after the Bhopal gas disaster) in the early 1960s. Principal producers are: Rhône-Poulenc; Drexel Chemical Company; Jin Hung; and Makhteshim-Agan. Carbaryl is processed by more than 290 formulators in over 1,500 different products[3,4].

In 1992 in the UK, it was the seventh most used active ingredient by weight on top fruit and was used on over 15,000 treated hectares on apples, pears and plums[5].

Health effects

Acute toxicity

Carbaryl is classified by the World Health Organisation (WHO) as 'moderately hazardous' (Class II)[6]. The acute toxicity varies considerably according to species and formulation. Estimates for the oral LD_{50} of the rat range from 200 to 850 mg/kg. Cats are sensitive to carbaryl with an LD_{50} of 150 mg/kg, whilst pigs and monkeys are less susceptible having an LD_{50} greater than 1,000 mg/kg[7].

Carbaryl can produce adverse effects in humans by skin contact, inhalation or ingestion. Its main mode of action involves the inhibition of the nerve enzyme cholinesterase and consequential disruption of the nervous system. The symptoms of acute toxicity are similar to other carbamates. Direct contact with the skin or eyes with moderate levels can cause burns. Inhalation or ingestion at high doses can be toxic to the nervous and respiratory systems resulting in nausea, stomach cramps, diarrhoea and excessive salivation, sweating, blurring of vision, lack of coordination and convulsions[8].

The US Environmental Protection Agency carried out a review of carbaryl-related poisoning between 1966 and 1980. During this period, 193 cases involving solely carbaryl and 144 cases which included carbaryl as one of the active ingredients, were assessed[9].

Workers have the greatest potential for exposure through inhalation or dermal absorption. The highest risk of exposure for the general public is through residues in food[10,11].

Manufacturing

On 3 December 1984 a gas leak containing methyl isocyanate (MIC) escaped from a Union Carbide factory in Bhopal, India. The MIC, an intermediate product used to make carbaryl, killed between 2,500 and 5,000 and injured about 200,000 (see PN26). A similar but smaller incident happened a year later at Union Carbide's plant in West Virginia which also produced carbaryl and aldicarb. In this case 135 people were injured[12].

Carcinogenicity

In 1987 carbaryl assessment by the International Agency for Research on Cancer (IARC) concluded that there were no data on cancer in humans and that the evidence of carcinogenicity in experimental animals was inadequate. This was reinforced in 1994 by a WHO Task Group report which concluded that most of the numerous cancer studies involving rats and mice were old and did not meet contemporary standards. The Group was aware that a pesticide company was carrying out new studies. Although they had not seen all the results, the Group was informed that these studies indicated significant increases in tumours at the highest dose in both rat and mice species. One of the main recommendations from the WHO report included a request that carcinogenicity studies meeting modern standards should be conducted[13].

In the UK, in November 1995, new company data indicated carbaryl could cause cancer in humans, although the research is not yet in the public domain. The studies were assessed by the Committee on Carcinogenicity and the Advisory Committee on Pesticides, which, in reporting to the government, concluded that it would be "prudent to consider carbaryl as a potential human carcinogen"[14]. The principal government response concerned the use of carbaryl against head lice in children. As a result, medicinal uses will only be available on prescription (see PN30 p.4).

Mutagenicity

Studies indicate that carbaryl is slightly mutagenic[15,16]. A WHO assessment concludes from available data that carbaryl does not pose a threat of inducing genetic changes in humans[17]. However, carbaryl can react with nitrite under certain conditions to form N-nitrosocarbaryl. This chemical is highly mutagenic at low levels in laboratory test systems. This may be of concern because nitrite can be found in food additives and human saliva which can react with carbaryl in the stomach to form N-nitrosocarbaryl[18].

Reproductive toxicity

The US EPA has concluded that carbaryl does not pose a teratogenic risk to humans[19]. However, it is considered to have endocrine disruptor effects[20].

Environmental effects

Carbaryl is lethal to many non-target species. The destruction of honeybee populations in sprayed areas is sometimes a problem. The insecticidal properties of carbaryl last for about 3-10 days. Degradation of carbaryl in the soil is mostly due to sunlight and bacterial action. It is bound by organic matter and can be transported by run-off. Carbaryl has a half-life of 7 days in aerobic soil and 28 days in anaerobic soil. In pond water, carbaryl has a half life of 1 to 32 days and it has been detected in groundwater in three separate sites in California[21].

Residues

Residues of carbaryl are regularly detected in tests on fruit and vegetables in the UK. In the latest report covering the period 1994, residues were found in dessert and cooking apples, grapefruit, ready prepared fruit-based baby food and lettuce. In none of these cases were the maximum residues limits exceeded[22]. Carbaryl is the tenth most commonly found pesticide in a 1994 total diet survey carried out by the US Food and Drug Administration[23].

Recommendations for use

Because of an announcement on 7 November by the UK government concerning its carcinogenic affects, carbaryl will no longer be approved for non-professional uses; will be available for medical uses only by prescription; and professional use is subject to restrictions designed to limit exposure. These are:

- applications must only be made using a vehicle with a closed cab;
- a low level induction bowl or closed systems must be used for transferring the product to the spray tank;
- coverall apron and gloves must be worn when handling the concentrate, (previously a face shield had also to be worn);
- coverall must be worn during application;
- coverall must be worn when handling contaminated surfaces;
- the latest time of treatment of top fruit is three weeks before harvest (previously it was seven days)[24].

Conclusion

At the end of 1995, the UK government's position on carbaryl changed, carbaryl is now considered to be a potential human carcinogen. Four main issues arise as a result:

- Given the health and safety and resistance concerns about alternative pesticide active ingredients in head lice preparations—malathion, permethrin and, less frequently lindane—there should be a review of all

head lice preparations containing pesticides.

- There remains considerable risk to agricultural and horticultural uses of carbaryl, as cited above. There should therefore be a label warning to indicate carbaryl is, in the view of the Advisory Committee on Pesticides, 'a potential human carcinogen'.
- Rodent carcinogenicity data, submitted by the manufacturer, is not in the public domain. A government full evaluation document on carbaryl should be made available promptly, particularly covering agricultural and horticultural use.
- The stringent protective clothing requirements imposed must call into question whether the safe use of carbaryl is possible in developing countries.

Paraquat

Paraquat is one of the most widely used herbicides in the world. It has had a tarnished reputation because of its acute oral toxicity and ill-health associated with operators—particularly in the plantation sectors of many developing countries.

What is paraquat?

Paraquat is one of the most widely used herbicides, and held the largest share of the global herbicide market until recently overtaken by glyphosate. Paraquat is sold in about 130 countries for use on large and small farms, plantations and estates and in non-agricultural weed control. It is a quick acting, non-selective herbicide, which destroys green plant tissue on contact and by translocation within the plant.

Paraquat was first synthesized in 1882. Its herbicidal properties were discovered only in 1955 in the ICI (now Zeneca) laboratories, who produced it commercially in 1961. This chemical type of herbicide—a bipyridyl—is shared with few other pesticides. One, the related diquat, is also a Zeneca product.

Although the patent protection on paraquat has expired, Zeneca remains the world's major producer. The raw bipyridyl and paraquat production take place in the UK (where a new £40 million production plant at Huddersfield replaced the original Widnes plant in 1995), in the US (Bayport, Texas) and Japan (Tal, 50% owned by Zeneca). Huddersfield is Zeneca's main plant, producing 8,000 tonnes a year, of which 95% is exported[1]. In addition paraquat production takes place in Brazil and India. Final stage manufacture takes place in Thailand and Kelang, Malaysia (Zeneca now has only a minority interest in the latter). The company has planned a US$80m. joint venture in China (north of Shanghai) to come on stream in 1998 and has recently said it will double the size of this plant to 6,000 tonnes a year[2]. Paraquat is made by other basic producers in Argentina, China, India, Spain, Taiwan and the US.

Zeneca markets paraquat as *Gramoxone* for agricultural use in formulations ranging between 24-36% active ingredient and for home and garden use under the trade names *Weedol* and *Pathclear* in formulations of about 2.5% paraquat. The biggest markets for the company's paraquat products are the US, Japan, Malaysia, Thailand, Mexico, France and Brazil and annual sales are still increasing[3]. For many years paraquat accounted for a big part of Zeneca's agrochemical sales (24% in 1987[4]) and is still a major product in the agrochemical portfolio.

Uses and usage

Paraquat is used to control broad-leaved weeds and grasses, being less effective on deep rooted plants such as dandelions. It does not harm mature bark, and is thus widely used for weed control in fruit orchards and plantation crops, including coffee, cocoa, coconut, oil palms, rubber, bananas, vines, olives and tea, ornamental trees and shrubs and in forestry. Other uses include weed control in alfalfa, onion, leeks, sugar beet, asparagus. It is used for weed control on non-crop land and can be used as a defoliant for cotton and hops before harvesting. Paraquat is used as a desiccant for pineapples, sugar cane, soya beans and sunflower[5]. In pineapples, for example, paraquat is applied after harvest to accelerate the drying out process and enabling plants to be burnt after 3-5 weeks, compared to 13 weeks after the alternative cutting and natural drying.

Paraquat is increasingly used to destroy weeds in preparing land for planting in combination with no-till agricultural practices which minimise ploughing and help prevent soil erosion. Although toxic to fish, it is used as an aquatic herbicide where it is absorbed by plant matter and silt.

Toxic effects

Acute toxicity

Paraquat is highly toxic to animals and has serious and irreversible delayed effects if absorbed. As little as one teaspoonful of the active ingredient is fatal. Death occurs up to 30 days after ingestion. Absorbed paraquat is distributed via the bloodstream to practically all areas of the body. The lungs selectively accumulate paraquat, and therefore contain higher concentrations than other tissues. This develops into pulmonary oedema and other lung damage, leading to fibrosis. Liver damage occurs and renal failure may follow as the kidneys remove absorbed paraquat.

At spray strength paraquat is of relatively low acute toxicity. It is classified as a solid and with an acute oral LD_{50} for rats of 157 mg/kg, which puts it into WHO as Class II 'moderately hazardous'[6]. Paraquat is also toxic if absorbed through the skin, see 'health issues' below. The minimum lethal dose by oral ingestion in human beings is about 35 mg/kg body weight, although less could be lethal without treatment. In dogs the lethal dose is 25-50 mg/kg and in cows and sheep 50-75 mg/kg[7]. There is no vapour toxicity, but it can cause nose bleeding if inhaled.

No antidote for poisoning exists although it is recommended that the highly absorbent Fuller's Earth is administered. Hospital care must be sought without delay.

Carcinogenicity

The US EPA has classified paraquat as a possible human carcinogen, but has concluded that the risks posed to individual applicators are minimal and of no concern[8].

Mutagenicity

The EPA requested additional studies on mutagenicity for re-registration in 1987. Of the studies of gene mutation accepted, eight were negative, four weakly positive and four were positive. Based on these the EPA concluded that paraquat is weakly genotoxic.

Ecotoxicity

Paraquat is less toxic to birds than to mammals. Its toxicity to fish varies with the species, size of fish and the softness or hardness of the water. Aquatic plants can concentrate high levels of paraquat, and a recent study indicates that significant tadpole mortality results when they feed on paraquat-contaminated plant material. It also resulted in tadpole tail abnormalities and affected feeding activity[9].

Key health issues

Being less acutely toxic at spray strength, the greatest risk to workers of fatal and serious accidents is during mixing and loading. Studies show high incidence of paraquat-related ill-health. For example a study in Guápiles, one of the main plantation regions of Costa Rica, identified 284 accident cases caused by paraquat between 1988 and 1990, including 123 cases of systemic poisonings, burns, eye injuries and fingernail damage[10].

Conditions of use in many developing countries mean it is difficult to follow label instructions and recommendations for use. Sprayers generally have no or inadequate protective clothing, lack training, and have little knowledge of the specific effects of products they use. On estates workers often spray for 10 months of the year, six days a week.

In occupational use the main route of exposure is through the skin and the worst cases occur during knapsack spraying. Continued exposure, as encountered by spray operators on plantations, is reported to affect the skin, eyes, nose and finger nails. Skin problems include mild irritation, blistering and ulceration, desquamation (peeling of the outer layer of the skin), necrosis (cell-death in skin tissue), dermatitis of the hands and in some cases scrotal areas (from leaking spray machines soaking trousers)[11]. Severe exposure on hands has resulted in nail damage, ranging from localised discoloration to temporary nail loss[12]. Eye splashes can result in irritation and inflamed eyelids (blepharitis) and visual acuity can decrease[13]. In Thailand workers received caustic burns on the feet after working with spinning disk applicators[14].

While small farmers in developing countries face some of the same problems as estate workers (lacking training and distant washing and medical facilities), they are exposed to paraquat less regularly and health problems are less severe. A study of small farmers in Kenya found no protective clothing was worn (the cost of a pair of rubber gloves was equivalent to a day's wage)[15].

Intact human skin is relatively impermeable to paraquat, although a number of fatalities resulting from dermal exposure to intact skin have been documented[16]. The presence of scratches, cuts, sores or severe dermatitis on the skin substantially increase the risks. Furthermore dermal exposure to paraquat can lead to skin injury including severe dermatitis, second degree burns and itching rash on the face, neck, hands or all over the body[17]. A study of Malaysian women plantation sprayers listed a range of health problems after exposure to paraquat[18]. An education worker with banana plantation workers in Honduras sent reports of common nose bleeds, diminishing eye sight, burning of skin, thinning of hair, nausea, loss of toe and finger nails[19].

Incidents also occur in the North. In 1992, a UK agricultural worker died after being splashed in the face with paraquat when he dropped an open container[20]. In 1994, a farmworker in the UK suffered a severe rash and infection to his groin after applying paraquat with a knapsack sprayer[21]. A similar incident was confirmed in 1992.

Poisoning: suicides and accidents

Accidental or deliberate ingestion of paraquat has been responsible for a large number of pesticide-related deaths. It is a major suicide agent in many developing countries. In Sri Lanka a 1989 study of 669 poison incidents indicated that agrochemicals were responsible for 59% and paraquat was the commonest poisoning agent with a fatality rate of 68%[22]. Paraquat poisonings are still common in the UK, where a study of pesticide poisoning between 1990-1991 indicates 44 deaths with paraquat responsible for 75%[23]. Many of these may be suicides. There is concern in developing countries that the easy availability of pesticides leads to suicides which might not otherwise occur. Most cases are self-poisoning, but not all intend to die[24].

To prevent accidental deaths, Zeneca added three alerting agents to the formulations. A stenching agent, was added to some formulations in 1975, an emetic to induce vomiting in 1977, and a blue dye to prevent confusion with cola, black coffee or other beverages was added from 1977. These are included in most but not all formulations depending on cultural acceptance and product registration.

Wildlife incidents

Incidents in the UK include paraquat (14 cases [11%] in 1994)[25], some of which are deliberate baiting of animals, while others involve exposure during or after spraying.

Measures to reduce exposure

In the US paraquat is a restricted use pesticide, and may be purchased and used only by certified applicators. In the UK there are no such restrictions and *Pathclear* and *Weedol* are allowed for amateur use in household gardens. Professional users should wear a protective face shield, wash splashes immediately, avoid spray drift and remove contaminated clothes immediately. The WHO Health and Safety Guide adds that normal personal protection and hygienic measures should be rigorously observed; paraquat should not be sprayed with inadequate dilution, nor used by people suffering dermatitis or with wounds[26].

Food residues

Residues in food are generally not detectable, except when it is used as a pre-harvest desiccant in food crops (e.g. cereals) where levels of up to 0.2 mg/kg of plant matter have been reported[27]. The Acceptable Daily Intake is recommended as 0.004 mg/kg/day body weight[28].

Environmental effects

Paraquat binds rapidly and tightly to clay particles in soils, and when adsorbed it is biologically inactive. It also binds to humus and other organic material: this results in no, or very low, soil residues or leaching into water sources.

Multiple spray trials showed paraquat residues in soil from 22-58 mg/kg. Under field conditions, the residual paraquat is slowly redistributed. Long-term field studies have shown degradation rates of 5-10% per annum, which is thought to prevent saturation of the carrying capacity of the soil and to prevent adverse effects on microflora and other soil organisms or on crop growth. In sandy soils with a low organic content paraquat may be more readily released into ground water[29].

The German federal biological institute (BBA) asserted in 1983 that repeated treatments of paraquat led to an accumulation in the soil and damage to crops. It refused to reregister paraquat products, but this was challenged in the courts by ICI. In 1992 the Court ruled that the BBA was justified but also ruled that registration should be granted to a new ICI formulation. However the formulation was restricted to only 10% paraquat; field crop applications are permitted only once every four years, and only in areas at risk from erosion. Wider registrations were refused because of effects on the environment[30].

Resistance

In contrast to less widely used herbicides, resistance has only occurred in 18 minor species on 50 sites, and nowhere is it of any agronomic or economic significance[31].

Conclusion

As paraquat binds quickly to soil, leaching into water sources is not generally a problem and its use as a herbicide does not lead to food residues. A major concern centres on accidental and deliberate ingestion of the active ingredient, where even small quantities are fatal. Exposure to the concentrated active ingredient is a problem during mixing and loading sprayers. In developing countries the conditions of use make safe use very difficult. Although not fatal at spray strength, regular use, such as required on plantations, leads to health problems.

Regulatory status

Finland and **Sweden** banned paraquat because of its high toxicity.

Austria banned because of high toxicity and high frequency of poisonings[32].

Hungary severely restricted because accidental poisoning rate was unacceptably high[33].

Norway voluntary cancellation.

Limited registration in **Germany**. Concern with residues in soil has led to registration for field crop applications only once every four years, and only in areas at risk from erosion.

US Restricted use pesticide— purchase and use only by certified applicators.

Europe Under EC Registration Directive 91/414 the UK will review paraquat on behalf of Member States by mid 1997[34]. ***(BD)***

Organophosphate insecticides

Organophosphate (OP) compounds are the most widely used group of insecticides in the world. Their acute toxicity causes a hazard both to professional and amateur users. In the UK, this has led to concern over OP use in sheep-dips, in agriculture generally and in the home. OPs are the commonest subject of questions asked by members of the public calling the Pesticides Trust information line. We have produced this fact sheet on OP insecticides in response to these concerns, and because this group has many similar properties.

What are OPs?

OPs were first recognised in 1854, but their general toxicity was not established until the 1930s. Tetraethyl pyrophosphate (TEPP) was the first OP insecticide, which was developed in Germany during World War Two as a by-product of nerve gas development[1].

OPs are all derived from phosphoric acid. They are generally among the most acutely toxic of all pesticides to vertebrate animals. They are also unstable and therefore break down relatively quickly in the environment. Altogether, over 100,000 OP compounds have been screened for their insecticidal properties, of which over 100 have been developed for commercial use. The Pesticides Trust holds details of 111 OPs on its active ingredient database.

OPs are nerve poisons which kill the target pest (usually insects). Most OP pesticides are insecticides, although there are also a number of related herbicide and fungicide compounds.

Uses and usage

OPs are marketed by many of the world's major agrochemical companies. Some of the main agricultural products are Hostathion (triazophos), Metasystox-R (oxydemeton-methyl), Dursban and Lorsban (chlorpyrifos), Sumithion (fenitrothion) and Actellic (pirimiphos-methyl)[2]. OPs have a wide range of pest control applications as contact, systemic and fumigant insecticides. Whilst widely used in agriculture, they are also used against household and catering establishment pests. They are used against head lice in humans and a number of ectoparasites in domestic animals. The aerial application of OPs (such as dimethoate) is permitted in the UK to control cereal and vegetable pests. Recently OPs have been in the news because of health concerns following their use in sheep dips, and as insecticides in military premises, on equipment and even on personnel during the Gulf War. The latest issue of Current Research Monitor provides a full list of OPs on the market.

World market

In 1992, global OP sales were US$ 2,880 million out of a total insecticide market of US$7,400 million. This makes OPs the most widely used group of insecticides, worth nearly 40% of the market—and they are likely to maintain dominance throughout the 1990s[3].

In the cotton growing industry where 22.5% of all insecticide use occurs, synthetic pyrethroid use overtook OP use in the early 1990s. By 1994, the synthetic pyrethroids accounted for 42.5% of the cotton insecticide market, with OP products still approaching 40%[4].

Developing countries

In developing countries OPs are widely used because they are cheaper than the newer alternatives. The Prior Informed Consent (PIC) procedure identifies pesticides banned, severely restricted or which cause 'problems under conditions of use under in developing countries' (PCU) to enable developing countries governments to prohibit imports if required. The PCU category is the hardest to identify as no regulatory decision has been made by a government. But, of the five that have now been identified all are OPs: parathion, methyl parathion, phosphamidon, monocrotophos and methamidophos.

UK usage

UK Farmers and growers regularly use OPs. They treated over a million ha with these products during 1994, representing a third of all insecticide applications. By weight of active ingredient, OPs represent about 60% of the UK arable insecticide market. A total of 395 tonnes were applied on arable farms in Britain during 1994[5]. Data on OP usage by value of sales is not readily available.

Between 1992 and 1994, usage of dimethoate increased by 89%, and chlorpyrifos by almost eight times—both were used to control aphids and orange wheat blossom midge levels, which had been unusually high[6].

Acute toxicity

OPs are generally acutely toxic. However active ingredients within the group possess varying degrees of toxicity. Minton and Murray have divided OPs into three groups. The first most and toxic group, e.g. chlorfenvinphos, has an LD_{50} in the range 1-30 mg/kg. The LD_{50} range for the second group, e.g. dichlorvos, is 30-50 mg/kg, and the least toxic group, e.g. malathion, has a range of 60-1,300 mg/kg[7].

OPs work by inhibiting important enzymes of the nervous system which play a vital role in the transmission of nerve impulses. Nerve impulses usually travel along neurons (nerve cells) by way of electrical signals. However, at a junction between two neurons (a synapse) and between a neuron and a muscle (neuromuscular junction) the impulse is transmitted in the form of a chemical substance (neurotransmitter). The neurotransmitter operating in the autonomic nervous system, neuromuscular junctions and parts of the central nervous system is acetylcholine which is released by cholinergic neurons. It is broken down and inactivated in milliseconds by the enzyme cholinesterase. With exposure to OPs, the enzyme is unable to function and a build-up of acetylcholine occurs, which causes interference with nerve impulse transmission at nerve endings.

In humans, poisoning symptoms include: excessive sweating, salivation and lachrimation, nausea, vomiting, diarrhoea, abdominal cramp, general weakness, headache, poor concentration and tremors. In serious cases, respiratory failure and death can occur.

Other consequences may follow high acute exposures. From one to several weeks after exposure, organophosphate—induced delayed neuropathy (OPIDN) [nerve damage] may set in. This may begin with burning and tingling sensations and progress to paralysis of the lower limbs.

Chronic toxicity

Neurological ef fects

Much attention has been focused on the chronic effect associated with occupational exposure of OP sheep dips. This is because exposure levels in this sector have been high. Exposure levels are also high in developing countries, which may mean chronic effects on sheep dippers in the UK are similar to those experienced generally in developing countries.

A number of studies have shown behavioural, psychological or electro-physical changes after exposure of humans or experimental animals to a number of OPs. There are also a number of studies which show no association[8].

Epidemiological studies have been carried out on the long term effects of OPs. One by Savage[9] showed OPs caused adverse response during psychometric testing and a test of motor reflexes, although it is not clear whether these effects were as a result of severe acute exposure. Another study carried out the by the Institute of Occupational Medicine in Birmingham suggested that subtle changes in the nervous system may be associated with exposure to OPs[10].

After assessing the available data, Dr Tim Marrs, Senior Medical Officer at the Department of Health concludes that we have not yet really answered the question: "is there a long-term effect of OPs on the central nervous system at sub-convulsive (low) doses?"[11].

A different view is taken by Dr Goran Jamal, a consultant neurophysiologist at the Southern General Hospital, Glasgow . He says there is experimental evidence that OPIDN may be more frequent among the users of OPs than previously thought. Dr Jamal notes: "Exposure to very small doses could result in cumulative poisoning which

may produce sub-clinical effects initially but render the individual susceptible to further toxic insults, thus producing progressive effects on the nervous systems[12]."

It is clear that more extensive research of low level occupational exposure to OP compounds is required. Little is known about the long-term neurological consequences of mild and repeated exposures which may have important health risks for those using these compounds.

Other effects

Psychiatric effects: Research reports have suggested that exposure to agricultural use of OPs produces depression, a major risk factor in suicides[13]. Research from Spain has shown that suicide rates are higher in areas of greater OP use[14].

Cardiac effects: A number of studies have drawn attention to cardiac effects associated with occupational exposure to OPs[15]. In a Health and Safety Executive publication (MS 17 December 1980) there is mention of "slowing of the heart with decreased cardiac output."

Professor William McKenna of St George's Hospital, London, believes that myocarditis (akin to a heart attack) can be caused after exposure to propetamphos, an OP sheep dip[16].

Teratogenicity (birth defects): There is conflicting evidence concerning the teratogenic effects of OPs in animals. Data on the effects of OP occupational exposure on pregnant women and their foetuses are not available[17].

Cancer: There is little evidence of strong mutagenic or carcinogenic effects in mammals from exposure to OPs. The exception is dichlorvos which the US EPA classifies in its C category as a possible human carcinogen, in which there is limited evidence of carcinogenicity in animals in the absence of human data[18].

Eye defects: Research from Japan and the US has found OP exposure during use in agriculture is related to an increase incidence of myopia (short-sightedness) and a more advanced ocular disease syndrome, Saku disease[19].

Areas of further research: There may be other chronic effects associated with OP exposure which are receiving current research interest. Firstly, there may be important but as yet un-characterised protein targets of OPs. Secondly, OP exposure may be affecting bone cells. The hypothesis is that chronic exposure to OPs carries the risk of developing severe metabolic bone disease[20].

Poisoning statistics

An accurate assessment of the numbers of people affected by OP use and misuse is impossible. The World Health Organisation estimates that there are in total three million acute severe cases of pesticide poisonings and 20,000 unintentional deaths each year, mostly in developing countries[21]. Of these poisonings a large (but unknown) proportion involves OPs. Poisoning data on OPs is difficult to come by in developing countries. An assessment by the Pesticides Trust revealed azinphos methyl, chlorpyrifos, methamidophos, methomyl, monocrotophos, parathion and phosphamidon have caused a number of health concerns in a range of developing countries[22].

In 1995, there were 15,300 pesticide poisoning cases in China, 91% of which were caused by OPs (67% were caused by just three OPs, parathion, methamidophos and omethoate)[23].

In 1995, Ciba withdrew its product Miral 500 CS product (isazofos) from 16 countries following three serious accidents in Africa and Latin America linked with its use[24].

Kyle Steenland at the US National Institute for Occupational Safety and Health maintains that acute poisoning from OPs remains a problem in industrialised countries. An estimated 3,000-5,000 cases of accidental poisoning occur annually in the US, according to the Environmental Protection Agency (EPA)[25].

An FAO study in Indonesia found that most symptoms associated with pesticide toxicity were significantly greater in the time of year when spraying occurred. Farmers sprayed often using mixtures of hazardous pesticides, and over 50% were OPs. This study was typical of OP poisoning in developing countries where it is impossible to match specific pesticides with symptoms[26].

Resistance

Resistance to OPs, first reported 14 years after their introduction, numbers 260 insect and mite species. Resistance to carbamate insecticides has appeared after five years, partly due to conditioning by previous OP exposure[27]. In November 1996 the first European case of sheep scab mite resistance to an OP (propetamphos) sheep dip occurred[28].

OPs in food

OPs are regularly detected at low levels in a range of food items. Usually residue levels are below the statutory maximum residue levels. OP residues found in UK carrots has proved a recent exception. Ministry of Agriculture, Fisheries and Food figures for 1995 showed that 1-2% of carrots contain OP residues up to 25 times higher than expected. OPs implicated included chlorfenvinphos, quinalophos and triazophos. In the higher residue samples, the acceptable daily intake was exceeded by up to three times[29].

OPs in the environment

OPs tend not to persist or bioaccumulate in the environment. They do however figure in many official cause-for-concern priority lists because of their toxicity, especially to the aquatic environment.

All OPs are part of the EU Black List, a priority list of the harmful chemicals set out in EU Directive 76/464/EEC which aims to protect the aquatic environment. The UK Department of the Environment classified dichlorvos, fenitrothion and malathion as Red List substances in 1989. The use of these chemicals should be reduced in order to combat environmental pollution[30].

Conclusion

By the late 1970s, the use of OPs began to overtake the organochlorine insecticides which included DDT. While organochlorines were relatively safe to use, their problem was persistence in the environment and detection in the human food chain. OPs on the other hand are more acutely toxic, but, do not persist in the environment beyond a few months. So with the switch from organochlorines to OPs, it can be assumed that the consumer has benefited at the expense of the pesticide operator.

In terms of sheep dips in the UK and OP use in developing countries, safer non-OP methods should be brought forward as a matter of urgency to reduce the risks to operators. There should be a moratorium on OPs until safer alternatives exist, and OP use should be severely restricted in developing countries where protective clothing cannot always be guaranteed. ***(DB)***

Benomyl

This fact sheet summaries the important health and environment effects of the fungicide benomyl. It came to the public's attention in the early 1990s because the exposure of pregnant women to benomyl was linked with subsequent eye defects in the foetus.

What is benomyl

Benomyl was first reported as a fungicide in 1968 and introduced onto the UK market in 1971 by the US company Du Pont[1]. It is a systemic benzimidazole fungicide that is selectively toxic to micro-organisms and to invertebrates, especially earthworms[2].

Benomyl and its main metabolite carbendazim bind to microtubules (an essential structure of all cells) and therefore interfere with cell functions such as cell division and intracellular transportation. The selective toxicity of benomyl as a fungicide is possibly due to its heightened effect on fungal rather than mammalian microtubules[3].

Uses and usage

Benomyl is used as a pre-harvest systemic fungicide, and as a post-harvest dip or dust. It combats a wide range of fungal diseases of arable and vegetable crops, apples, soft fruit, nuts, ornamentals, mushrooms, lettuce, tomatoes and turf. It is also available widely for amenity and amateur garden use[4]. Benomyl's principal trade name is Benlate.

The basic manufacturer is Du Pont Agricultural Products, based in Wilmington, Delaware. Global figures of benomyl usage are not widely available. In Britain benomyl was applied to 22,157 ha of top fruit crops (1992)[5]; 2,957 ha of bulb and flower crops (1994)[6]; 1,359 ha of outdoor vegetable crops (1995)[7] and 1,033 ha of hardy nursery stock (1993)[8].

Acute toxicity

Benomyl is of such a low acute toxicity to mammals that it has been impossible or impractical to administer doses large enough to establish an LD50. It therefore has an arbitrary LD50 that is 'greater than 10,000 mg/kg/day for rats'. However, skin irritation may occur with workers exposed to benomyl[9]. It is a mild to moderate eye irritant and is a skin sensitiser. Florists, mushroom pickers and flower growers have reported allergic reactions to benomyl[10].

In 1992, benomyl exposure caused adverse occupational health effects (headaches, diarrhoea and sexual dysfunction) in agricultural workers in Florida[11].

Chronic toxicity

In a laboratory study, dogs fed benomyl in their diets for three months developed no major toxic effects but did show evidence of altered liver function at the highest dose (150 mg/kg). With longer exposure, more severe liver damage occurred including cirrhosis after two years[12].

Carcinogenic effects

The US Environmental Protection Agency classified benomyl as a possible human carcinogen[13]. There is an element of doubt in this classification because carcinogenic studies have produced conflicting results. A two year experimental mouse study has shown it probably caused an increase in liver tumours. The Ministry of Agriculture Fisheries and Food (MAFF) takes the view that this was bought about by the hepatoxic effect of benomyl[14].

Reproductive effects

Tests on laboratory animals have shown benomyl can have an effect on reproduction. In one rat study, where the mothers were fed 1,000 mg/kg/day for four months, the offspring showed a decrease in viability and fertility[15]. In studies to investigate the effects of benomyl on male reproductive performance, fertility was reduced at all dose levels tested. In another study a no-effect level of 15mg/kg/day was established based on testicular abnormalities[16].

Permanent reductions occurred in the size of testes and male accessory glands in 100 day-old offspring from female laboratory rats receiving 31.2 mg benomyl/kg body weight per day. Rats developed a reduced sperm activity following acute inhalation exposure, acute and sub-chronic oral exposure. The same effect occurred in dogs following a single four hour inhalation exposure[17].

Eye defects

In 1993, the *Observer*, a UK national newspaper, published the first in a series of articles alleging a possible link between exposure of pregnant mothers to benomyl and their children being born without eyes (anophthalmia) or with related syndromes including reduced eyes and blindness due to severe damage of the optic stem[18]. The newspaper cited a number of suspected clusters in the UK that may have corresponded to areas of benomyl use.

Government officials at MAFF made an assessment of the claims but concluded it was doubtful there was a link. They said likely benomyl exposure in the pregnant mothers was not sufficiently high to cause developmental eye problems in their children. MAFF concluded: "The no effect level for teratogenicity based on all the available data was 30mg/kg/day. The exposure of both operators and consumers is several orders of magnitude lower than this no-effect level. It is therefore difficult to see how any link can be made with eye defects and exposure to benomyl."[19]

Studies have shown that eye defects can occur at relatively high doses. A test in which rats were dosed orally demonstrated evidence of microphthalmia at dose levels of 62.5 mg/kg and above[20].

At the height of concern over benomyl, councillors on Lincoln's Environmental Committee urged local farmers to adopt a voluntary ban on the use of benomyl.

In 1996 a Miami jury awarded US$4 million to a child whose mother was exposed in pregnancy to Benlate. The child was born without eyes. The mother in this case was subject to an unusually high dose of Benlate. The case is on appeal by the manufacturers. An important issue in the case is whether the timing of exposure—during the formation of the optic nerve in the foetus—is critical as well as the magnitude of exposure. A Benlate compensation case involving an English boy from Essex born without eyes is also due to be heard shortly in the US[21].

Mutagenic effects

There are conflicting negative and positive results making it difficult to form a definite conclusion relating to mutagenicity. Two papers show that benomyl causes an increased incidence of chromosomal aberrations. In a range of *in vitro* assays there was evidence that benomyl caused aneuploidy (a chromosome abnormality). Other results show it is not mutagenic[22].

Environment

Benomyl binds strongly to soil and does not dissolve in water to any great extent. When applied to turf, it has a half-life of three to six months, and when applied to bare soil the half-life is six to 12 months[23].

Resistance

Resistance to benzimidazole fungicides in general has reduced the market share of benomyl in recent years. Benomyl was the first truly systemic fungicide and originally showed a wide range of activity against pathogens in many different crops[24].

Crop damage claims in Florida

In 1991, many US growers blamed Benlate DF for destroying millions of dollars worth of crops. Growers placed as many as 1,900 damage claims against the manufacturers Du Pont, mostly involving ornamental crops in Florida. The reason for the crop damage is not clear. The Florida Department of Agriculture suggested Benlate was contaminated with dibutylurea and sulfonylurea herbicides. A non-pesticide theory suggested that unusual weather was also a contributory factor.

After many years of legal wrangling Du Pont paid out about US$750 million in damages and out-of-court settlements. By 1993, a coalition of farm worker and environmental groups came together to form Benlate Victims Against Du Pont that called for a nation-wide boycott of Du Pont products.

After carrying out tests, Du Pont denied that Benlate was contaminated with dibutylurea and sulfonylureas and stopped compensation pay-outs. In 1995, a Florida judge rejected a complaint from the Florida Department of Agriculture that had alleged such a link[25]. The affair continues

to inflict financial repercussions on Du Pont. The third quarter results in 1996 included a US$47 million charge relating to the Benlate recall[26].

Conclusion

The main area of concern with benomyl involves its chronic effects. At high doses, adverse effects such as eye birth defects occur after exposing experimental animals to the fungicide. MAFF says people are unlikely to receive such doses and therefore conclude it is safe. This issue raises two questions: is there a safe level of exposure, and is the timing of the exposure during pregnancy critical?

As yet, national regulatory authorities have not taken a precautionary approach and banned benomyl on health grounds. An alternative, Azoxystrobin, may be coming onto the market. It is based on a natural fungicide and may prove to be safer than benomyl. However, it will probably be more expensive, and follows a chemical-for-chemical replacement strategy that may not be successful.

Methyl parathion

Methyl parathion is an organophosphate (OP) insecticide that has caused many health problems—particularly in developing countries—since its introduction onto the market in the early 1950s. This fact sheet provides information on the hazards associated with methyl parathion, focusing also on recent restrictions on its application in the US, implemented because of misuse of the product .

What is methyl parathion?

Methyl parathion was originally developed by the German pesticide company Bayer. It is a non-systemic pesticide that kills pests by acting as a stomach poison.

It is used to control chewing and sucking insects in a wide range of crops, including cereals, fruit, vines, vegetables, ornamentals, cotton and field crops[1]. Methyl parathion is generally applied as a spray, mainly as an emulsifiable concentrate formulation. The recommended application rates are 15-25g of active ingredient per 100 litres[2].

Usage

The basic manufacturers of methyl parathion are All India Medical Co (India), Bayer India, Bayer Mexico, Cheminova (Denmark), Rallis India and Sundat (Singapore)[3]. In 1993, other production facilities existed in Brazil, the former East Germany, China and the former USSR. Although not used in the UK, methyl parathion is widely used throughout the world, and is registered in at least 38 countries[4].

Information on global sales and production data are not widely available. For the financial year 1995-96, India produced an estimated 2,200 tonnes of technical grade methyl parathion[5].

Cheminova, a major producer, sells US$ 15 million per year in the US, one of its key markets for this product[6]. Overall the company recorded a 10% rise in sales in 1996. Its forecasts for future growth in methyl parathion have however been affected by an agreement to withdraw certain formulations in the US (see below)[7].

Acute toxicity

The World Health Organisation classifies methyl parathion as a class Ia 'extremely hazardous' pesticide[8]. It is highly toxic by inhalation and ingestion, and moderately toxic by dermal adsorption (it is also readily adsorbed through the skin). The oral LD_{50} in rats is 2.9-35 mg/kg, in mice is 33.1-119.5 mg/kg, in rabbits is 19-420 mg/kg and dogs is 50 mg/kg. The dermal rat LD_{50} is 44-67 mg/kg[9].

Like other organophosphate insecticides, methyl parathion is a cholinesterase inhibitor (see the Organophosphates fact sheet PN34 pp20-21). When inhaled, the first adverse effects are a bloody or runny nose, coughing, chest discomfort and difficulty breathing. Skin contact may cause localised sweating and involuntary muscle contractions. Following exposure by any route, other systemic effects may begin within a few minutes, or be delayed for up to 12 hours. These may include pallor, nausea, vomiting, diarrhoea, abdominal cramps, headache, dizziness, eye pain, blurred vision, constriction or dilation of the pupils, tears, salivation, sweating and confusion. In severe cases, poisoning will affect the central nervous system, producing in-coordination, slurred speech, loss of reflexes, weakness, fatigue, and eventual paralysis of the body extremities and respiratory muscles. Death may be caused by respiratory failure or cardiac arrest[10].

Chronic effects

Effects reported in workers repeatedly exposed to methyl parathion include impaired memory and concentration, disorientation, severe depressions, irritability, confusion, headache, speech difficulties, delayed reaction times, nightmares, sleepwalking, drowsiness and insomnia[11].

There are no epidemiological studies on effects related only to methyl parathion exposure[12].

Cancer

The International Agency for Research on Cancer evaluated methyl parathion in 1983, and concluded that the available data do not provide evidence that methyl parathion is carcinogenic to experimental animals. No data on humans were available[13].

Mutagenicity

Mutagenicity tests have been both positive and negative. The results of most of the *in vitro* studies with both bacterial and mammalian cells were positive[14].

Food

The WHO recommended that more definitive studies should be conducted on residues of methyl parathion in fresh foods[15]. Residues are regularly detected in a range of fruit and vegetables. In the UK during 1995, researchers found residues in imported celery, dessert grapes and oranges, all below maximum residue limits [16].

Fate in the environment

Methyl parathion has a half-life in aqueous solution of 175 days[17], and 10 days to two months in soils[18]. The rate of degradation increases with temperature and with exposure to sunlight. When large concentrations of methyl parathion reach the soil, as in an accidental spill, degradation will occur only after many years[19].

The US Environmental Protection Agency (EPA) may have detected 4-nitrophenol, a methyl parathion breakdown product, at very low levels in drinking water wells. The EPA is uncertain and cannot quantify the amount or frequency of 4-nitrophenol in drinking water because the analytical technique is not reliable[20].

Methyl parathion is unlikely to bioaccumulate.

Wildlife

Methyl parathion is highly toxic for aquatic invertebrates with most LC_{50}s ranging from <1 µg/litre to about 40µg/l[21]. In 1992, a massive bird kill occurred in Costa Rica after it was applied by plane in a cotton field[22]. Methyl parathion has been implicated in the deaths of waterfowl in Spain and the acute poisoning of fish, birds, cattle and wild animals in the Sudan[23].

Hazards in developing countries

Conditions in developing countries make it extremely difficult to associate a particular active ingredient with a poisoning incident.

In the early 1950s the manufacturers introduced a powder formulation of methyl parathion which caused problems because of the poor conditions of use in developing countries. Methyl parathion became the mainstay of pest control in cotton, and very quickly there were hundreds of poisonings from this single product, and reportedly dozens of fatalities[24].

In Oarana State, Brazil, pesticide incidents compiled by the Toxicological Information Centre and Health Clinics noted 1,243 incidents involving methyl parathion between 1982-1991[25].

There is evidence that methyl parathion is not used safely in Central America. Research carried out in 1996 shows that methyl parathion caused a number of documented poisonings among agricultural labourers involved in Nicaraguan cotton production. In some cases they have ended up in hospital with classic OP poisoning[26].

Cheminova, the Danish manufacturers of methyl parathion, says it only sells to developing countries if they carry out 'safe farming'. However, researchers on the ground in countries like Guatemala and Nicaragua say methyl parathion is rarely used safely.

The WHO has set out a number of safety remarks for methyl parathion use:

- methyl parathion may only be used by trained personnel;
- A field sprayed with methyl parathion may not be entered for 48 hours after application;
- methyl parathion may not be sprayed by hand;
- people may not be used as markers when spraying from the air[27].

There is evidence that these recommendations are broken in developing countries[28].

Problems in the US

Recently, there have been a number of important US prosecutions involving methyl parathion. Over 1,500 homes and businesses

in Mississippi and Ohio were sprayed with methyl parathion by unlicensed operators. Methyl parathion is not permitted for use indoors in the US. The authorities had to relocate over 1,100 people in temporary accommodation, and clean up costs could reach US $50 million. In addition, local vets reported deaths of household pets due to methyl parathion exposure[29].

These events led the US EPA to cancel the registrations of emulsifiable concentrate formulations. These came into effect on 30 April 1997, following a voluntary agreement with the US registrants, led by Cheminova. Cheminova is to carry out a public education programme on the proper use of the insecticide[30].

Mississippi case

On 13 March 1997, Dock Eatman, Sr of Moss Point Mississippi was convicted by a jury of illegal spraying of the insecticide methyl parathion in homes and other buildings in the Pascagoula (Miss.) area in 1995 and 1996. Eatman did not have a licence for commercial pesticide application. This insecticide is only approved for outdoor agricultural use. Eatman faces a maximum of 21 years in prison and/or up to US $2.1 million in fines. This case is being investigated by the EPA's Criminal Investigation Division, the FBI and authorities from the state of Mississippi[31].

Ohio case

Lutellis Kilgore of Elyria Ohio, was also charged on 21 March 1997 with illegal use of methyl parathion. He allegedly applied the insecticide in a manner inconsistent with its label to more than 60 properties without an application certificate. The spraying led to a US $20 million publicly-funded clean up of the affected properties. Kilgore faces a maximum of one year in prison and/or a fine of up to US $100,000 for the illegal application and five years in prison and/or a fine of up to US $250,000 for making false statements to federal investigators[32].

Restrictions

Methyl parathion is banned in Indonesia, Sri Lanka and Tanzania, and is severely restricted in Colombia, Korea, China and Japan. It is one of five pesticides identified for inclusion in the Prior Informed Consent Procedures of the Food and Agriculture Organisation on the grounds of causing problems under conditions of use in developing countries.

Conclusions

As a hazardous OP pesticide, methyl parathion is regularly misused in developing countries. The measures taken recently in the US should help to reduce potential problems, but they merely highlight the difficulties of using such a product in conditions like Central America, where protective clothing and training are often lacking or ineffective. As a result, methyl parathion should be more severely restricted in developing countries. *(DB)*

Chlorpyrifos

Chlorpyrifos was originally marketed in the US in the 1960s and is now one of the word's leading insecticides. More recently concerns about related health effects have led to restrictions on its use.

What is chlorpyrifos?

Chlorpyrifos is one of about 100 organophosphate (OP) insecticides on the market today. It is used to kill insect pests by disrupting their nervous system. Chlorpyrifos has an advantage over other products in that it is effective against a wide range of plant-eating insect pests.

Production

Chlorpyrifos (trade name Dursban, Lorsban and others) is primarily produced by the US multinational DowElanco. Other manufacturers are Aimco, Agriphar, Excel, Ficom, Gharda, Lupin, Montari (all India), Frunol (Germany), Jin Hung (South Korea), Point Enterprises (Switzerland) Luxembourg and Makhteshim-Agan, (both Israel). DowElanco protects the compound from generic competition vigorously and in 1995 received compensation form Micro Flo who, DowElanco claimed, had used DowElanco data to obtain US registration without paying for the data[1].

Uses and usage

Chlorpyrifos is the world's leading insecticide in volume terms[2]. It was first reported in the scientific literature in 1966, and was originally developed by Dow Chemical Co. (now Dow Elanco)[3]. This OP is used extensively in the US, in agriculture, and both inside and outside the home environment. In agriculture, it is used primarily on corn (maize), alfalfa and cotton.

Figures on usage are not generally available. In the US, the *Journal of Pesticide Reform* indicated that during the mid-1990s, 9-12 million pounds (4-5.5 million kg) were used annually in non-agricultural situations in over 17% of households. Agricultural usage estimates vary even more with annual application anywhere between 10 and 21 million pounds (4.5-10 million kg)[4].

In the UK, chlorpyrifos is more commonly used in agriculture, although no really accurate figures are available for use in the home.

During 1997 about 100,000 kg were used on about 50 different agricultural crops. Those most heavily dosed in descending order were grassland, wheat, spring barley, desert apples and culinary apples[5]. Chlorpyrifos is registered for household use against ants and wasps, and by professional users for use in food storage areas against insects[6].

Acute toxicity

The acute oral LD_{50} (the dose required to kill half of a population of laboratory test animals) for chlorpyrifos is between 135-165 mg/kg for rats[7]. It is classified by the World Health Organisation as a Class II, 'moderately hazardous' pesticide[8].

Chlorpyrifos and other insecticide OPs are inhibitors of anticholinesterase (ACh-ase), an enzyme vital to the nervous systems of animals and humans. The transmission of impulses across certain nerve junctions (including, in humans, those of the autonomic nervous system) involves the release of a transmitter chemical, acetylcholine (ACh). The stimulant effect on ACh is rapidly cancelled by ACh-ase activity. The inhibiting effect of OPs on ACh-ase results in sustained high levels of ACh with consequent serious and widespread disruption of nervous activity.

Chlorpyrifos is one of the leading causes of acute insecticide poisoning in the US, according to the US Environmental Protection Agency (EPA)[9].

Symptoms of acute chlorpyrifos poisoning in humans include headache, nausea, dizziness, muscle twitching, weakness, increased sweating and salivation, and occur when cholinesterase activity has been reduced by about 50%. Unconsciousness, convulsions, and death can result with sufficient exposure. These symptoms are common to all organophosphate insecticides with delayed symptoms one to four weeks after exposure of numbness, tingling, weakness and cramping in the lower limbs which can progress into paralysis[10] (see also PN34 fact sheet on OPs).

Effects on the central nervous system may include confusion, drowsiness, depression, difficulty concentrating, slurred speech, insomnia, nightmares, and a form of toxic psychosis resulting in bizarre behaviour[11].

Chlorpyrifos poses a risk of serious damage to eyes, and is irritating to skin[12]. Poisoning via the skin can easily be misdiagnosed suggesting some cases of occupational exposure are missed[13]. The dermal LD_{50} for rabbits is about 2,000 mg/kg[14].

Chronic effects

The adverse effects of OPs are currently the subject of much debate in the UK. A recent government report concluded that their potential to cause ill health following long-term low-level exposure remains unknown and subject to controversy[15].

Repeat or prolonged exposure to chlorpyrifos may result in the same effects as acute exposure, including the delayed symptoms. Other effects reported on workers repeatedly exposed include impaired memory and concentration, disorientation, severe depression, irritability, confusion, headache, speech difficulties, delayed reaction times, nightmares, sleepwalking and drowsiness or insomnia. An influenza-like condition with headache, nausea, weakness, loss of appetite and malaise has also been reported[16].

In 1996, the Multiple Chemical Sensitivity Referral and Resources in the US cited cases of over 450 adults and children who were poisoned by the pesticide in their home or workplace. Their most common symptoms were chronic headaches, nausea and vomiting, breathing difficulties, vision problems, neuromuscular pains and multiple chemical sensitivity[17].

In 1997, the US EPA announced a *Risk Reduction Plan for Chlorpyrifos* which included restrictions on its use because of a number of alleged ill-health effects cases. They included 22 reports of alleged nervous system disorders and 35 cases that alleged sensitivity to the chemical[18] (see also Restriction below).

Birth defects

According to the US EPA, it is not known whether chlorpyrifos can affect reproduction or cause birth defects in people, although these potential problems have been the subject of much debate[19]. In 1996, a national coalition of US environmentalists[20] called on the EPA to issue emergency regulations restricting the use of Dursban because of concerns that it could cause birth defects.

An independent scientific study reported four cases of serious and disabling birth defects seen in children whose mothers were exposed to Dursban during the first three months of their pregnancy. These children have deformed heads, faces, eyes and genitals—and require constant care. The report concluded that "exposure to Dursban is consistent with a common teratogenic (birth defect) agent. The production of similar defects in animals exposed to Dursban and its components supports this teratogenic connection[21]."

Cancer

The US EPA classification indicates that chlorpyrifos shows no evidence of carcinogenicity[22]. However, according to the *Journal of Pesticide Reform*, xylenes, used as solvents in some chlorpyrifos-containing products, have caused increased rates of leukemia among exposed workers. Xylenes may also be co-carcinogens and increase the number of skin cancers caused by other carcinogens in laboratory animals[23].

Effects on the immune system

Recent research has identified immune system abnormalities in individuals following chlorpyrifos exposure. Higher than usual frequencies of allergies and sensitivities to antibiotics together with atypical abundances of certain types of lymphocytes (decreases in T cells and increases in CD26 cells) were found in patients one to five years after chlorpyrifos exposure. Increased expression of CD26 cells is associated with autoimmunity, where an individual's immune system acts against itself, rather than against infections[24].

Children

Recent US research showed that if a child played in his/her home a week after chlorpyrifos application, there was a danger that he/she would be overexposed to chlorpyrifos. The researchers were still finding chlorpyrifos residues on toys two weeks after application[25]. Based on the findings of this and other research, the estimated

chlorpyrifos exposure levels from indoor spraying for children are about 21-119 times above the US-recommended reference dose of 3 µg/kg/day from all sources[26].

Food residues

A national survey of pesticides and their metabolites in the US found that the primary chlorpyrifos breakdown product, 3,5,6-trichloro-2-pyridinol was the second most commonly detected chemical in food[27].

Chlorpyrifos is regularly detected in UK fruit and vegetables. The latest report for 1997 shows that one sample out of 15 of Spanish celery was detected at 0.06 mg/kg which exceeded the maximum residue limit of 0.05 mg/kg[28].

Environmental fate

Chlorpyrifos is relatively non-persistent in the environment. However, aquatic invertebrates, particularly crustaceans and insect larvae are sensitive to exposure. The LC_{50}s for these species are generally less than 0.1 µg/litre[29].

Restrictions on use

In 1997, the EPA, in conjunction with manufacturers, designed policies to reduce exposure in the home, especially to children. They agreed to eliminate chlorpyrifos concentrates that require mixing, limit household consumer use to ready-to-use products, and prohibited use in inappropriate areas (toys, curtains and furnituture)[30].

Conclusion

In common with other OPs, chlorpyrifos usage has raised a number of concerns during the 1990s. Most of the examples of ill-health problems originate from the US. However chlorpyrifos is used widely throughout the world, and it is likely that many US exposure conditions can be related to the rest of the world.

Glufosinate ammonium

Glufosinate is produced by AgrEvo, a joint venture established by the German chemical corporations Hoechst and Schering. Current usage levels raise concern because of the marketing of genetically engineered crops resistant to this herbicide.

Glufosinate is produced at Hoechst's Frankfurt plant in Germany where work began in 1995 to double production capacity in anticipation of the launch of genetically engineered glufosinate resistant crops.

The herbicide was first introduced into Japan in 1984. In the UK, glufosinate was first considered in 1984. It was not approved then for toxicological reasons, but was given provisional approval in 1991 (see below). US registration was achieved in 1993. The product is now registered for use in more than forty countries and is marketed under a number of trade names including Basta, Rely, Finale and Challenge.

In the UK agriculture, relatively small amounts of glufosinate are used: 25 tonnes on 60,000 ha. The main crops are oilseed rape and potatoes[1]. These figures may change dramatically if genetically engineered, glufosinate resistant crops are commercialised.

In North America, commercialisation has already begun. AgrEvo recently launched a formulation called Liberty, a glufosinate product for use on crops resistant to glufosinate. In Canada, Liberty Link canola has been on sale since 1995. In 1997, Liberty Link soybean and maize were approved in the US. The US maize and soybean herbicide markets account for 40% of all US pesticide sales[2].

AgrEvo expects glufosinate to become its linchpin product by 2000, with an annual turnover of about US$680 million by 2001-2[3]. AgrEvo aims to promote the fast spread of glufosinate resistance into popular crop varieties, including sugar beet. The profits could be considerable: introduction of Liberty Link varieties is expected to increase sales of glufosinate to over US$300 million[4].

What is glufosinate

Glufosinate is a short name for the ammonium salt, glufosinate-ammonium. It is a broad-spectrum contact herbicide and is used to control a wide range of weeds after the crop emerges or for total vegetation control on land not used for cultivation. Glufosinate herbicides are also used to desiccate (dry off) crops before harvest.

Glufosinate is a natural compound isolated from two species of Streptomyces fungi. It inhibits the activity of an enzyme, glutamine synthetase, which is necessary for the production of glutamine and for ammonia detoxification. The application of glufosinate leads to reduced glutamine and increased ammonia levels in the plant tissues. This causes photosynthesis to stop and the plant dies within a few days[5]. Glufosinate also inhibits the same enzyme in animals.

Health impacts

Hoechst claims that under conditions of recommended use of glufosinate ammonium, a "detrimental effect on the health of both users and consumers is extremely unlikely"[6]. Glufosinate ammonium structurally resembles glutamic acid, a natural amino acid that can stimulate the central nervous system. It is recognised that excess release of glutamic acid results in the death of nerve cells in the brain[7].

The surfactant, AES, which is used in formulations, has also been found to cause toxic effects and may be a cause of some of the clinical symptoms observed in suicide cases involving glufosinate. The metabolite, MPPA-3, is, like glufosinate, a neurotoxin. The US EPA reported that MPPA-3 injected into the brain of rats caused severe convulsions[8].

Acute Toxicity

The toxicity of glufosinate varies in different laboratory animals. The oral LD_{50} is 436-464 mg/kg in mice and 1,510-1,660 mg/kg in rats. Dogs are the most sensitive. They can be twice as susceptible as mice (the LD_{50} for beagles is 200-400 mg/kg[9]). The LD_{50} of the surfactant, AES, is 1,995-2,138 mg/kg in rats. The World Health Organisation (WHO) classifies glufosinate in toxicity Class III, "slightly hazardous". The WHO classification system is based on the LD_{50} for rats and aims to take account of the sensitivities of more vulnerable test animals.

The dermal LD_{50} for glufosinate is about the same as for oral exposures. However, through the skin, glufosinate formulations can be 2.5 times more toxic than glufosinate alone[10]. Glufosinate was first considered by the UK Ministry of Agriculture, Fisheries and Food (MAFF) Scientific Sub-Committee in 1984. The herbicide was refused approval because of the toxicity of the formulation (containing 30% surfactant) when absorbed through the skin[11].

In 1991, The Scientific Sub-Committee recommended "Provisional Approval for six products for five years with a data submission deadline of three years subject to a number of specific conditions and label amendments"[12]. However, the Sub-Committee remained concerned about the dermal toxicity of one of the six formulations, requiring the applicants to submit further studies.

Neurotoxic Effects

Glufosinate has been found to cause a number of neurological symptoms in laboratory animals following both oral and dermal exposure. At lethal doses, overt signs of toxicity include: convulsions, salivation, hypersensitivity, irregular breathing, and trembling[13]. Some of the behavioural changes lasted several days[14].

At sub-lethal doses, glufosinate can have significant, but not so easily observable impacts. For example, a recent study found that low doses of glufosinate affected central nervous system development in young rats. One-day old rats were exposed to a dose of 1, 2 or 5 mg/kg of glufosinate daily for seven days. At six weeks they were tested for the 'wet-dog shakes' induced by administering kainic acid. Kainic acid stimulates glutamate receptors in the brain. The frequency of wet-dog shakes decreased significantly in all the glufosinate exposed rats. The results suggested that exposure to even low doses of glufosinate in the infantile period in rats causes changes in the kainic acid receptor in the brain[15].

Teratogenic effects (birth defects)

In recent studies, sub-lethal doses of glufosinate ammonium was found to cause abnormalities in the development of embryos in mammals both *in vitro* and *in vivo*. Deformities in the brain were the main finding of these studies:

- Mouse embryos exposed to glufosinate *in vitro* developed apoptosis (fragmentation of the cells leading to cell death) in the neuroepithelium of the brain[16]. An earlier study found that all the embryos in the treated groups had specific defects including overall growth retardation, increased death of embryos, hypoplasia (incomplete development) of the forebrain at 10 µg/ml, and cleft lips at 20 µg/ml[17].
- The effects on embryos after exposure of pregnant rats to glufosinate during the time of neurogenesis (central nervous system development) was determined. Pregnant rats were injected subcutaneously with 3 or 5 mg/kg of glufosinate once daily from days 13-20 of gestation. The results suggested that glufosinate exposure at a crucial stage in pregnancy causes a decrease in the number of glutamate receptors in offspring[18].

Residues in food and water

Residues in food are an area of concern, especially when glufosinate is used as a pre-harvest desiccant. MAFF in the UK states that adult consumers are most likely to be exposed to residues of glufosinate in potatoes and dried (or processed) peas and in liver and kidney from animals fed on contaminated cereal straw[19]. The WHO/FAO recommended acceptable daily intake (ADI) for glufosinate is 0.02 mg/kg.

MAFF's 1990 evaluation document on glufosinate states that when it is used as a desiccant, glufosinate residues will be found in dried peas, field beans, wheat, barley, oilseed rape, and linseed. The highest likely residue levels in commodities for human consumption were considered to be: 3 mg/kg in peas, 1 mg/kg in wheat grain, and 0.5 mg/kg in oilseed rape. The reported residue levels in animal feed were high, including 50 mg/kg in barley straw and pea stalks and 20 mg/kg in wheat straw and field bean stalks.

MAFF reported that when wheat grain containing residues was turned into flour, 10-100% of the residue was retained. Residue levels in bran were 10-600% of those in grain.

Genetic modification and herbicides don't mix

In the UK, relatively small amounts of glufosinate are currently used. This may change dramatically if genetically engineered, glufosinate resistant crops are commercialised here.

AgrEvo claims that "application of gene technology can reduce the impact of agriculture to the environment". The evidence, however, suggests otherwise.

An application for the registration of glufosinate resistant sugar beet in Germany is expected soon. So far, research has not demonstrated that glufosinate resistant sugar beet offers improved yields, quality or cost effectiveness.

The development of herbicide resistant crops is a strategy developed by a number of chemical companies to increase profits and ensure that key product lines can compete in the market place.

Studies (summarised in the table) demonstrate that the product may pose a number of hazards. The introduction of glufosinate-resistant crops and a greater exposure to glufosinate increases the likelihood of these harmful effects in humans and the environment. Glufosinate resistance will tend to intensify and increase dependency on herbicide use rather than lead to significant reductions.

AgrEvo's Claims	Independent Research Findings
Glufosinate is safe for users and consumers	• Glufosinate and its metabolite, MMPA-3 are neurotoxins • Glufosinate effects the central nervous system development in young rats • Teratogenic effects of glufosinate include growth retardation and deformities of the brain in rats and mice • The surfactant in glufosinate formulations is also toxic
Glufosinate is not a threat to drinking water	• Glufosinate is persistent and mobile in soils • Under some soil conditions (eg sandy soils which overlie many aquifers) glufosinate is highly persistent and mobile
Glufosinate is environmentally safe	• Glufosinate is toxic to beneficial soil micro-organisms and is a threat to wild plant communities • Glufosinate is toxic to some aquatic organisms • Glufosinate may increase nitrogen leaching from arable fields
Glufosinate resistant crops will reduce the impact of agriculture on the environment	• Herbicide-resistance will intensify dependency on herbicide use rather than lead to any significant reductions • Glufosinate resistant crops are likely to lead to glufosinate resistant volunteers, weeds and feral populations • Foreign genetic material may be introduced into wild populations and effect the structure of plant communities

Source: References cited on page 23 and in Health and Environmental Impacts of Glufosinate (Details available from the Pesticides Trust)

In addition, MAFF found that the use of glufosinate as a herbicide and/or a desiccant in potato crops can lead to residues in the tubers in the order of 0.1 mg/kg.

In 1991, the MAFF Advisory Committee on Pesticides, the body responsible for registering pesticides in the UK, was concerned that significant residues of glufosinate were found in the crops at the time of harvest[20]. In particular, they were concerned that residues of 'additive ingredient' and the metabolite, MPPA-3, were found in milk and the tissues of animals fed treated straw. The Sub-Committee proposed a restriction on straw feeding to reduce health risks to livestock and consumer intakes of residues in animal products.

AgroEvo claims that glufosinate is unlikely to leach into groundwater[21], but independent evidence suggests otherwise. Glufosinate is highly soluble in water and is also classified as persistent and mobile (see below). The dangers of soluble pesticides contaminating water supplies as a result of recommended agricultural use is recognised by both the industry and governments throughout the European Union.

Environmental Fate

The US Environmental Protection Agency (US EPA) classifies glufosinate ammonium as 'persistent' and 'mobile'. Degradation of glufosinate is largely by microbial activity. The half life has been determined in numerous laboratory studies and varies from 3 to 42 days in some studies[22] and up to 70 days in others[23]. The shortest half life tends to be in soils with a high clay and organic matter content[24].

In one study, residues of glufosinate were found in spinach, radishes, wheat and carrots planted 120 days after glufosinate had been applied[25]. In sandy soils, which overlie many aquifers, glufosinate has been found to be highly persistent due to lack of biodegradation. Its transport through the soil was also determined to be 'essentially unretarded' [26]. Glufosinate's metabolite, MPPA-3, has been found to be more persistent and more mobile than glufosinate[27].

Effects on wildlife

Very little information is available on the effects of glufosinate on aquatic and terrestrial wildlife. Most of the experimental work to date has been produced as a requirement of registration and has focused on the lethal dose rates for different organisms. Information on the sub-lethal effects of glufosinate on plants or animals is sparse. Researchers at the Department of Animal Ecology, Justus-Liebig University, Germany, are concerned about the lack of data on the impacts of glufosinate in the environment. They are particularly concerned about the commercialisation of glufosinate resistant crops and say "it has become a matter of urgency to make a study of the behaviour of this substance [glufosinate] in conjunction with natural systems" [28].

Glufosinate is toxic to a number of aquatic animals including the larvae of clams and oysters[29], daphnia and some freshwater fish species[30]. The commercial formulations are more toxic than the technical grade glufosinate. For example, for the aqueous formulation, the LC_{50}s for the fish tested were between 12.3 and 79 mg/l and for the active ingredient they were between 320 and 1,000 mg/l[31]. The rainbow trout, *Oncorhynchus mykiss*, was the most sensitive species in these tests.

The acute oral LD_{50} for birds is 2,000 mg/kg. 4 day old partridges given a dose of 2,000 mg/kg of 96% glufosinate showed signs of central nervous system damage including ataxia, disequilibrium, convulsions, trembling, and wing flapping[32].

Effects on non-target plants

Glufosinate is a broad spectrum herbicide and is damaging to most plants that it comes into contact with. The US EPA has stated that glufosinate is "expected to adversely affect non-target terrestrial plant species" [33].

Conclusion

The development of herbicide resistant crops is a strategy developed by a number of chemical companies to increase profits and ensure that key product lines can compete in the market place. AgrEvo has targeted the broad spectrum herbicide, glufosinate, as their linchpin product for the future and initiated a fast track programme to produce a range of crops resistant to glufosinate. However, studies demonstrate that it causes adverse health effects in animal studies, is likely to leach to drinking water sources, could increase nitrate leaching, and is toxic to beneficial soil micro-organisms. The introduction of glufosinate resistant crops and a greater exposure to glufosinate increases the likelihood of these harmful effects in humans and the environment. Glufosinate resistance will tend to intensify and increase dependency on herbicide use rather than lead to significant reductions.

This fact sheet is taken from Health and Environmental Effects of Glufosinate (in press) written by Topsy Jewell for Friends of the Earth.

References see page 23.

Dicofol

Dicofol is a organochlorine acaricide (a chemical that kills mites) that is structurally similar to DDT. It is highly toxic to aquatic life and can cause egg-shell thinning in some bird species.

Production

Dicofol first appeared in the scientific literature in 1956[1], and was introduced onto the market by the US-based multinational Rohm & Haas in 1957[2]. Other current manufacturers include Hindustan (India), Lainco (Spain) and Makhteshim-Agan (Israel)[3]. It is sold under a number of trade names, including Kelthane and Acarin.

DDT is one of the intermediate products produced during dicofol manufacture. In 1986, the US Environmental Protection Agency (EPA) temporarily cancelled the use of dicofol because relatively high levels of DDT contamination were ending up in the final product. Modern processes can produce technical grade dicofol that contains less than 0.1% DDT[4].

Uses

Dicofol is used to kill crop-feeding mite pests such as the red spider mite. It is a contact poison which kills the pest after being ingested and picked up from the surface of the crop. In many countries, dicofol is also used in combination with other pesticides such as the organophosphates parathion-methyl, and dimethoate[5].

Application figures are not generally available as most countries do not record usage data according to particular active ingredients. The UK data show the average amount of dicofol active ingredient used between 1994 and 1997 was 1,143 kg per year[6]. It is approved for use on apples, pears, blackcurrants, hops, strawberries, and protected crops of cucumbers, tomatoes and ornamentals[7].

In the US dicofol is mostly used on cotton, apples and citrus crops. Other crops include strawberries, mint, beans, peppers, tomatoes, pecans, walnuts, stonefruit, cucurbits, and non-residential lawns/ornaments[8]. During 1998 the manufacturers voluntarily cancelled all residential turf uses[9]. Based on available US data from 1987 to 1996, total annual domestic agricultural usage of dicofol averaged 390,000 kg of active ingredient for 290,000 hectares treated. The largest markets for dicofol in the US are cotton (over 50%) and citrus (almost 30%). Most of the usage is in California and Florida[10].

Acute toxicity

The acute oral LD_{50} (the dose required to kill half a population of laboratory test animals) for dicofol is 595-690 mg/kg for rats. It is classified by the World Health Organisation as a Class III, 'slightly hazardous' pesticide[11].

Like many insecticides and acaricides, dicofol is a nerve poison. The exact mode of action is not known, although in mammals it causes hyperstimulation of nerve transmission along nerve axons (cells). This effect is thought to be related to the inhibition of certain enzymes in the central nervous system[12].

Symptoms of ingestion and/or respiratory exposure include nausea, dizziness, weakness and vomiting; dermal exposure may cause skin irritation or a rash; and eye contact may cause conjuctivitis. Poisoning may affect the liver, kidneys or the central nervous system. Very severe cases may result in convulsions, coma, or death from respiratory failure[13].

Dicofol can be stored in fatty tissue. Intense activity or starvation may mobilise the chemical, resulting in the reappearance of toxic symptoms long after actual exposure[14].

Occupational exposure

The US EPA reviewed dicofol under its reregistration eligibility decision (RED) programme in 1998 which raised some strong concerns over hormonal and development toxicity for mixers, loaders, applicators, and field workers[15]. In particular the EPA is concerned about exposures to handlers during the treatment of crops by ground and aerial equipment, and during treatment of ornamentals using hand-held equipment[16].

There are very few accurate estimates of occupational ill health from exposure to pesticides. Some figures are available from the US and the UK.

The California Department of Food and Agriculture has one of the world's most extensive incident reporting systems. Between 1982 and 1992, 38 incidents involving dicofol alone were reported: systemic 19 (50%); skin 10 (26%); eye 8 (21%); and eye/skin 1 (3%). The number of incidents per 1,000 applications for all illnesses ranged from 0.11 to 0.21.

The US National Pesticides Telecommunications Network database collected reports from 1984 to 1991 showing 91 human, 9 animal and 31 other poisoning incidents for a total of 131 incidents involving dicofol from 571 phone calls made to the hotline[17].

In the UK two cases in recent years were confirmed by the Pesticides Incident Appraisal Panel, although this does not necessarily reflect the true number of incidents involving dicofol. In one incident, a woman suffered inflammation and irritation to the skin around her left eye after exposure to dicofol and tetradifon. In another case, a four-year-old boy developed a cough after the field of hops adjacent to his garden was sprayed with a number of pesticides, including dicofol[18].

Neurotoxicity

Dicofol produced neurotoxic effects in adult rats in neurotoxicity tests. The US EPA has also identified that a postnatal development neurotoxicity study in rats is required in order to fill current data gaps[19].

Chronic effects

Tests on laboratory animals show that the primary effects after long term exposure to dicofol include increases in liver weight and enzyme induction in the rat, mouse and dog. There are also effects relating to altered adrenocorticoid metabolism (part of the hormonal system). In the rat hormonal changes were accompanied by the histological observation of vacuolation (empty cavities) of the cells of the adrenal cortex[20].

The US EPA has classified dicofol as a Group C, possible human carcinogen. There is limited evidence that it may cause cancer in laboratory animals, but there is no evidence that it causes cancer in humans. This classification was based on animal test data that showed an increase in the incidence of liver adenomas (benign tumour) and combined liver adenomas and carcinomas in male mice[21].

Residues in food and water

An assessment of dicofol by the UK Pesticides Safety Directorate in 1996 found that residues in apples, pears, blackcurrants and strawberries were higher than expected. The assessors considered it likely that the acceptable daily intake may be breached under normal conditions of use. Because of data gaps, they also found that implications are not clear for data on the transfer of residues from hops into beer, from blackcurrants into blackcurrant juice and apples into apple puree[22].

There is no established US maximum contaminant level (MCL) or health advisory levels for residues of dicofol in drinking water[23]. In the European Union, the maximum level is the same for all active ingredients 0.1 µg/litre (parts per billion [ppb])[24].

Cumulative effects

As part of the RED review, US regulators have to assess all available information concerning the cumulative effects of pesticide residues and other substances that have a common mechanism of toxicity.

Dicofol is classed as an organochlorine pesticide. Other members of this class include DDT, methoxychlor, chlorbenzilate and ethylan. Less closely related members include lindane, dieldrin, endrin, chlordane, heptachlor, aldrin, endosulfan, kepone and toxaphene[25]. Currently the US EPA does not have available data to determine whether dicofol has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment[26].

Endocrine disruption

The US RED review concludes that evidence for dicofol to cause endocrine disruption is suggestive, but not definitive. It has reproductive effects in some species (see below), although they appear to differ somewhat from its close analogues DDT and/or DDE. Whether the difference is due to the ability of dicofol to be metabolised to less toxic chemicals, its relatively short half-life (compared to DDT/DDE), or the reduced potency of the parent compound, is not currently known[27].

In 1980, an accident at the US Tower Chemical Company led to a release of dicofol into Lake Apopka in Florida. Ten years later Dr Guillette of Florida University linked this incident to a subsequent decline in the fertility of alligators in the lake. The US EPA is still not clear whether dicofol is involved in the reproductive failure of the alligator population following the accidental spill[28].

In 1993, US scientists reported the presence of dicofol in water samples from the western San Joaquin Valley in California. The highest concentration 2,500 ng/litre (2.5 ppb) was found at Orestimba Creak following agricultural spraying in the area. The researchers were concerned about these levels and called for further research into the endocrine-disruption toxicology of chemicals dissolved in water at low concentrations[29].

Environmental fate

According to the US Department of Agriculture, dicofol has a half-life in the environment of 60 days[30]. Other US EPA laboratory and field studies show that dicofol has a half-life ranging from days to months. In ecological monitoring studies conducted in New York, Florida and California, dicofol dissipated from the soil surface with a half-life ranging from two to four months. The chemical is likely to be more persistent in acidic than neutral or alkaline soils or waters[31].

Dicofol and DDT are similar chemical structures, and the US EPA considers that dicofol has to a lesser degree some ability to accumulate in the environment[32].

Wildlife

Analytical screening of wildlife tissue samples for organochlorine chemicals rarely includes dicofol, and this may explain why, compared with other organochlorines, the relative hazard of dicofol to wildlife populations is poorly known[33].

Dicofol is 'highly' to 'very highly' toxic to a range of aquatic organisms, including fish, invertebrates and estuarine/marine organisms[34]. The 96 hour LC_{50} for Channel catfish is 0.30 mg/litre (parts per million [ppm]), 0.51 mg/l for bluegill, 0.183 mg/l for fathead minnow, and 0.12 mg/l for rainbow trout[35]. It also causes early life stage toxicity at levels of 19 ppb for fathead minnow and 1 ppb for rainbow trout[36]. Little information is available on bioaccumulation in fish species[37].

Estuarine/marine organisms are particularly susceptible to dicofol. The 96 hour LC_{50} for the eastern oyster embryo larvae is 15.1 µg/l ppb, 0.14 mg/l (ppm) for mysid shrimp, and 0.37 ppm for sheepshead minnow[38].

In birds, dietary concentrations of dicofol between one and 10 µg/g (wet weight) fed to captive adult females caused eggshell thinning, reduced hatching success, or reduced fertility in American kestrels *(Falco sparveruis)* and eastern screech-owls *(Otus asio)*[39]. Similar effects have also been noted in the mallard duck and ring dove[40]. Researchers in the US are concerned that there have been no intensive field investigations of possible reproductive effects, despite the results from these laboratory findings[41]. Because of its potential to bioaccumulate in the environment, the US EPA has requested that chronic reproduction testing is required[42].

Regulation

In 1990, the use of dicofol was suspended in Sweden for environmental reasons[43]. In Switzerland its use is permitted for research purposes only[44]. Throughout the European Union dicofol containing less than 78% pp'-dicofol or more than lg/kg (0.1%) of DDT or DDT related compounds cannot be used[45].

The 1998 US EPA review of dicofol recommended a number of changes in order to protect the environment and wildlife. Dicofol applications are limited to no more than one per year. In the UK, the maximum number of treatments permitted is two per year for apples and hops, and two per crop for strawberries, protected crops and tomatoes[46].

When the UK Advisory Committee on Pesticides reviewed dicofol in 1995, it was also concerned about occupational exposure, and made some recommendations:

- To minimise exposure, personal protective equipment is required when handling the liquid products, and contaminated surfaces during/after application.
- All liquid products, with one exception, must be packed in 'wide neck' packs to minimise potential exposure.
- All hand held uses are banned[47].

Conclusion

Environmental concerns have prompted progressive countries like Sweden to ban dicofol, and other countries are following suit by imposing severe restrictions on its use.

Nevertheless dicofol is one of the world's last organochlorines still in widespread use. It has perhaps survived because its environmental persistence is low relative to DDT, although this is not the case when compared with the vast majority of other pesticides on the market. DDT is after all one of the lowest of all common denominators. ***(DB)***

Tridemorph

Tridemorph is a systemic fungicide that first gained commercial clearance in 1969[1]. An evaluation document to be published later in the year by the UK's Pesticide Safety Directorate (PSD) will report concern over its potential reproductive effects on spray operators. Until recently there has been very little human health and environmental information in the public domain on this active ingredient, yet it is used widely over numerous crops in many countries around the world.

What is tridemorph

It is used to control the fungus *Erysiphe graminis* in cereals, *Mycosphaerella* species in bananas, and *Caticum solmonicolor* in tea. Tridemorph is formulated with the fungicide carbendazim, to extend its spectrum of use in cereal disease control[2]. It is also used with a number of other fungicides including: cyproconazole, fenbuconazole, fenpropimorph, flusilazole, propiconazole, tebuconazole, triadimenol[3].

Tridemorph is applied onto many crops across the world, but very little data on usage and production is in the public domain. It was developed in the 1960s by the German multinational BASF who sell tridemorph under the trade name Calixin. In Europe, it is used in Austria, Belgium, Finland, Germany, Greece, Italy, Ireland, Luxembourg, Netherlands, Spain and UK[4]. It is applied widely on banana plantations Latin America, especially Costa Rica and Ecuador[5].

In the UK there are 29 approved products, predominately for use against powdery mildew on cereals but also on root crops. There are no home garden products[6]. In 1997, tridemorph was most commonly used on winter barley (61,207 kg) followed by wheat (50,588 kg) and spring barley (18,411 kg)[7].

Acute toxicity

The acute oral LD_{50} (the dose required to kill half a population of laboratory test animals) for tridemorph is 650 mg/kg for rats. It is classified by the World Health Organisation as Class II a 'moderately hazardous' pesticide[8]. It is harmful if swallowed and irritating to eyes and skin[9]. Tests show it is moderately to severely irritating to rabbit skin and rabbit eyes. Prolonged or repeated exposure may cause dermatitis and/or conjunctivitis. Inhalation of tridemorph vapour may cause adverse health effects (specific effects not stated). Laboratory rats survived an 8 hour exposure to air saturated with tridemorph vapour[10].

Chronic effects

Until recently, very little data was in the public domain. On 19 March 1999, Jeff Rooker the UK Agriculture Minister announced that the use of tridemorph would be restricted due to concerns over its reproductive effects. PSD, an executive agency of the Ministry of Agriculture, Fisheries and Food (MAFF) has considered the data under the UK Review Programme, and will produce a full evaluation later in the year. The Advisory Committee on Pesticides, which advises UK Ministers on pesticide safety, considered PSD's review of tridemorph in February 1999 and made a number of recommendations (see below)[11].

Reproductive effects

Ministers and officials at MAFF became concerned after BASF, the main manufacturer of tridemorph, provided new information that identified a possible risk of harm to the unborn child if the mother is exposed to tridemorph while working with the chemical. The company submitted its data as part of its obligation under the Food and Environment Protection Act 1985 to provide any new information on the potentially dangerous effects of a pesticide product. The data comprised developmental toxicology studies in the rat and rabbit, and a literature review of developmental studies *in vivo* and *in vitro*.

PSD assessed these studies and concluded that tridemorph was capable of inducing abnormalities, primarily cleft palate, during the development of the rat foetus. In rabbits, it did not appear to be teratogenic. Scientists at PSD consider this difference was not addressed, and from the available information, it was not possible to determine whether the effects seen in rats would be produced in humans. They were nevertheless worried about the severity of effects, the steepness of a dose response curve they had produced and absence of a clear no observed adverse effect level (NOAEL) in the rat developmental study. The officials found it necessary to apply an increase safety factor in establishing the acceptable daily intake for consumers (ADI), acute reference dose for consumers (ARfD), and admissible operator exposure level (AOEL). Based on this data PSD set the following end-point values based on the rat development study with a safety factor of 1,000 fold:

- A temporary ADI of 0.01 mg/kg, based on the minimal effect of 10 mg/kg body weight per day
- An AOEL of 0.01 mg/kg bw/d
- An ARfD of 0.01 mg/kg bw/d

For many teratogenic compounds, adverse effects on foetal development can be produced by a single exposure at a crucial period during pregnancy. According to PSD, this was an important factor when considering those working with products containing tridemorph.

Furthermore, the studies showed that the AOEL was exceeded when exposures to operators, resulting from the use of products containing tridemorph, were estimated. Although PSD said it was possible to reduce these exeedances by imposing requirements for the use of additional personal protective equipment (PPE), making changes to the maximum application rates of products, and imposing a requirement to apply products only via tractors in closed cabs; the possibility of single exposures resulting from splashes and spillages during mixing and loading would still present a significant risk to women of child bearing age. On this basis, the Agriculture Minister specified the following requirements, following advice from PSD and the ACP:

- All approval holders should carry out an active information campaign to alert users of the products to the fact that the use of tridemorph by women of child bearing age may carry a risk of adverse reproductive effects. This includes warnings on the labels of products.
- Closed transfer systems must be used when transferring formulations containing tridemorph from the container to the spray tank.
- Application formulations containing tridemorph must be restricted to vehicles where the operator is protected by a closed cab.
- For all formulations containing tridemorph, the maximum individual dose must not exceed 375g active ingredient per hectare. Approval for uses were revoked where the maximum individual dose exceeded this limit.
- The following additional PPE requirements were specified for all formulations containing tridemorph:

  Operators must wear suitable protective gloves when handling contaminated surfaces.
- The packaging for all formulations containing tridemorph was restricted to 'wide-neck' containers only.

Other reports of reproductive effects

In 1995 tridemorph was listed as teratogenic (a substance that may cause birth defects) in Sax and Lewis Dangerous Properties of Industrial Materials[12]. It has also been identified as a potential endocrine disruptor by Germany's Federal Environment Agency[13] because of concerns over its effect on mammalian ovaries. In 1990 the US publication Pest Line reported: "Embryoethality, cleft palate and other anomalies, and maternal toxicity were reported in a study of pregnant rats and mice."[14]

Environmental fate

In rats, following oral consumption, tridemorph is rapidly absorbed, and is almost completely eliminated within two days. Residues in cereal grains at harvest are <0.05 mg/kg. Its half-life in soils has been measured at 20-50 days in laboratory tests, and 14-34 days in field tests[15].

It is not often detected in water because of the lack of adequate analytical techniques. In the UK, the Working Party on the Incidence

of Pesticides in Water noted in 1996 that it was one of the most significant widely used fungicides for which methodology was lacking[16].

Tridemorph is harmful to fish and/or other aquatic life. Users are reminded not to contaminate surface waters or ditches with the chemical or used container[17]. The LC_{50} [the concentration required to kill half a population of laboratory test animals] (96 hr) for trout is 3.4 mg/litre[18].

For bees, the LD50 (24 hr) is >200µg-bee[19].

Data gaps

In the UK, MAFF requires that further data (unspecified) from the approval holders to supplement the existing data package (see also above Reproductive effects)[20].

Conclusions

There is little data about tridemorph in the public domain. After years of use, PSD is only just about to publish an evaluation. The substance will not be reviewed by the European Union under the Registration Directive. The US EPA has no factsheet, nor has the US academic source Cornell University, which publishes a number of factsheets on pesticides on the net. No evaluation on toxicology or food residues has been published by Codex, the joint UN FAO/WHO food standards agency and there are no MRLs for food. Notwithstanding the lack of data, in the UK, tridemorph was the 18th most widely used active ingredient (by area) on arable crops in 1996, and the 23rd by weight[21]. ***(DB)***

Aldicarb

Aldicarb is a carbamate pesticide that has been used around the world since the mid 1960s. Public interest groups consider it hazardous enough to include it in the Pesticide Action Network's Dirty Dozen list.

What is aldicarb

Aldicarb is a systemic pesticide (readily taken up by the roots and transferred around the plants) and acts as a contact stomach poison. Aldicarb is applied to the soil to control chewing and sucking insects (especially aphids, whitefly, leaf miners, and soil-dwelling insects), spider mites and nematode worms. It is used in production of in sugar beet, fodder beet, strawberries, potatoes, onions, hops, soya, citrus fruit, bananas, coffee, sorghum, pecans, cotton, and cane sugar.

Production

Union Carbide, the original patent holder, was the sole aldicarb producer until 1987, when the company sold its worldwide agrochemical division to Rhône-Poulenc (RP) of France. Today the chemical is still a major part of RP's sales strategy. In the first quarter of 1998, aldicarb sales were second only to RPs flagship insecticide fipronil[1].

Problems in production and transport

In 1984, the gas leak at a Union Carbide factory in Bhopal killed 3,000 local residents. The factory was making the carbamates aldicarb and carbaryl for the Indian cotton crop. Many thousands have since suffered respiratory ill effects. At the time of the gas escape, all safety systems designed to contain leaks were out of action[2].

Eight months after the Bhopal disaster, a gas leak at a Union Carbide aldicarb factory in West Virginia, sent 125 people to hospital[3].

In April 1994, a truck carrying 23,000 pounds (10,500 kg) of aldicarb crashed near Dallas, US, spilling the toxic pesticide and sending at least 17 people to hospital. The truck hit a traffic sign and burst into flames. Officials on the scene evacuated a five-mile radius around the incident site, including two schools and dozens of homes[4].

Usage

Data on pesticide usage by active ingredient is hard to come by. The US State of California is an exception, where all pesticide use is recorded. Here the use of aldicarb more than doubled between 1991 and 1997 from 190,707 pounds (87,000 kg) to 530,066 pounds (240,000kg)[5].

In the UK, most aldicarb is used on potatoes, followed by sugar beet, carrots and parsnips. Overall, usage has steadily declined since the early 1980s, and in 1998 an estimated 56,500 kg was applied to a range of arable, fruit, glasshouse, vegetable and fodder crops[6]. The market share of aldicarb used on potatoes is much higher in the UK than in any other EU member state[7].

Acute toxicity

As a member of the carbamate group, aldicarb is an anticholinesterase compound. This means it acts as a nerve poison by disrupting nerve impulses.

The acute toxicity of aldicarb is probably the highest of any widely used pesticide in the UK[8] and the US[9]. It is classified by the World Health Organisation (WHO) as a Class Ia 'extremely hazardous' pesticide. The acute oral LD_{50} (the dose required to kill half a population of laboratory test animals) for aldicarb is 0.93 mg/kg[10].

The acute skin LD_{50} for male rabbits is 20 mg/kg[11]. Rats were killed within five minutes by a dust concentration of 0.2 mg/litre air[12].

The symptoms of aldicarb poisoning in humans are characteristic of other organophosphate and carbamate insecticides. In humans, signs of aldicarb poisoning include dizziness, salivation, excessive sweating, nausea, abdominal cramps, vomiting, diarrhoea, blurred vision, pin-point pupils, difficulty breathing and muscle twitching. Death follows if exposure has been high enough (at levels see above)[13].

Atypical of carbamates in general, aldicarb is extremely toxic through both the oral and dermal routes. This is one reason aldicarb is only formulated in a granular mix (10-15% active ingredient) rather than as an emulsified concentrate or a liquid, as is the case with many other pesticides. Aldicarb is less toxic when administered in the dry granular form (lethal concentration $(LC)_{50}$ in the range of 7.0 mg/kg). Despite this the US authorities still place aldicarb well within the range of category I 'highly toxic' poisons, and it has to carry the words 'Danger—Poison' on the label[14]. In the UK by contrast the formulation is registered as: 'Toxic in contact with the skin, by inhalation and if swallowed'[15]. In the US, a formulation that can contain up to 15% aldicarb active ingredient is used; in the UK the figure is only 10%. According Rhône Poulenc: "Temik 10G is marketed in the UK as a formulation which contains aldicarb at a concentration of 10% of the active ingredient. In addition aldicarb is made less hazardous formulating it as a solid granule formulation. For these reasons the product is classified by the Pesticides Safety Directorate as 'toxic'[16]. According to WHO classification tables, a formulation containing 10% means the product is downgraded to Ib 'highly hazardous' from Ia 'extremely hazardous'[17].

Chronic effects

The International Agency for Research on Cancer (IARC) considers there is evidence of genetic mutation in animals[18]. In the UK, the Advisory Committee on Pesticides reviewed aldicarb in 1994 and considered it is not a human genetic hazard[19].

Immunological effects

In 1986, epidemiologists in the US found that consumption of low levels of aldicarb contaminated well water was associated with one immune system abnormality (an indication of this is an increase in the number of 'T8 cells' [lymphatic white blood cells]). Tests in laboratory mice also found water contaminated with as little as one part per billion of aldicarb affected one parameter of immune function, the plaque forming cell response[20]. The results of this study have been widely debated among regulators internationally.

Environmental fate

The potential exposure of aquatic animals is high due to aldicarb's solubility and mobility in soil. Aldicarb, applied to farm fields can be transported to aquatic areas through run-off, especially for sandy soils. Its half-life in water can be as long as a few months[21]. There are long harvest intervals for aldicarb for treated crops because of environmental persistence. In the UK, the harvest interval for potatoes it is 8 weeks[22].

Wildlife

Aldicarb has a broad spectrum action and can affect a range of beneficial insects[23]. It is also dangerous to animals, including game and wild birds, and fish or other aquatic life[24]. The 96 hour LC_{50} for rainbow trout is 0.88 mg/l, and for blue-gill sunfish 1.5 mg/l. It is also toxic to bees[25].

Residues in food

In California during the mid 1980s there were a number of outbreaks of food poisoning involving water melons and cucumbers caused by aldicarb. The estimated doses of the residue ranged between 0.0011 and 0.06 mg/kg body weight, and most were well below the 0.025 mg/kg Lowest Observed Effect Level for blood cholinesterase depression (a measurement of adverse effects from aldicarb). Workers at the Californian Department of Health Services concluded from these cases that: "Aldicarb appears to be more toxic than previously suspected"[26].

At least 30 people were poisoned in Ireland in May 1992 after eating cucumbers contaminated with aldicarb. The Irish Department of Agriculture took a week to identify the chemical, which was not approved for use on cucumbers[27]. A further Irish incident occurred in 1993 when a boy, aged 15, fell ill during a football match. Doctors established that he had aldicarb poisoning after eating cucumber that had wrongly been applied by a local farmer[28].

In the UK aldicarb residues have been found at levels below the maximum residue limit in citrus fruit. In 1995, one sample out of 71 imported oranges contained residues of aldicarb[29].

Aldicarb residues in individual potatoes may exceed MRLs due to the factor of variability (see PN 43 p.7), even though the crop may have been treated in accordance with good agricultural practice[30].

Data gaps

In 1998 the European Commission Scientific Committee on Plants carried out a review of the health and environmental effects of aldicarb. It recognised that, across Europe as a whole, very little residue data is available.

The committee outlined a number of data gaps in relation to dietary and environmental risk assessment:

- Further individual commodity residue data for the relevant crops should be generated from European field trials.
- The data available for aldicarb are not adequate to allow a comprehensive health risk assessment to be made for operator exposure.
- The risk assessment for the exposure of smaller sized birds to granules critically depends on the assumption that more than 99% of the granules are incorporated into the soil. Whilst this may be achieved under ideal conditions, the Committee believes that this high degree of incorporation is not consistently achievable under normal agricultural use. The Committee therefore advised that a reassessment is necessary.
- The notifier (Rhône Poulenc) submitted no data on aldicarb and its metabolites (aldicarb sulfone and sulfoxide) relating to long-term toxicity for aquatic and soil dwelling organisms, and oral toxicity and exposure assessment for honey bees.

In conclusion, the Committee was not able to assess, from the data available, whether the use of aldicarb should continue pending the generation, submission and evaluation of additional data[31].

Developing country problems

Adverse effects of pesticides are often difficult to assess in developing countries. Groups participating in the international Pesticide Action Network (PAN) survey have identified aldicarb as 'known to have caused health or environmental problems' in Sudan, Colombia, Costa Rica and Ecuador[32].

A member of the Dirty Dozen

Aldicarb is one of the PAN's Dirty Dozen pesticides. PAN took this action because of the deaths, poisoning and environmental contamination in both developing and industrialised countries caused by this pesticide[33].

Regulatory action

In 1990 Rhône Poulenc announced a voluntary halt to the sale of Temik (aldicarb) in the US for use on potatoes because of concerns about groundwater contamination and because residue levels were significantly exceeding the maximum legally permissible residue limit. By 1992 the Environmental Protection Agency (EPA) approved the re-introduction of aldicarb on this crop in limited geographical areas. This decision was based on extensive data showing that new application technologies and other restrictions resulted in lower residues in food. Despite these controls, aldicarb remains in the EPA's intensive Special Review process because of continuing concerns of risks to groundwater. Indeed, aldicarb's use on potatoes is only approved in areas where the risk of groundwater is believed to be low[34].

In 1997, the French Ministry of Agriculture introduced rigorous new measures requiring registrants of aldicarb-based insecticides to provide quarterly statements of amounts sold and their purchasers. Distributors of aldicarb also had to supply details of names, addresses and final destinations to French agriculture officials[35].

As an anticholinesterase compound, aldicarb is being reviewed by the UK Pesticide Safety Directorate and the Health and Safety Executive.

Conclusion

One of the PAN Dirty Dozen, aldicarb has caused concern among public interest groups around the world since the mid 1980s. These worries appear to have been echoed by the European Union, which has come out with a series of important questions over the health and environmental effects of this chemical.

Aldicarb is one of the few active ingredients that has been implicated in food poisoning in northern countries.

As a matter of urgency, its use should be severely restricted, and more research should be initiated to find safer alternative methods of pest control. ***(DB)***

Endosulfan

Endosulfan is an organochlorine insecticide and acaricide, and acts as a contact poison in a wide variety of insects and mites. Endosulfan is effective against a wide range of insects and certain mites on cereals, coffee, cotton, fruit, oilseeds, potato, tea, vegetable and other crops[1]. It can also be used as a wood preservative.

Endosulfan is sold as a mixture of two different forms of the same chemical (alpha- and beta-endosulfan). Its colour is cream to brown and it smells like turpentine[2].

Endosulfan is a highly toxic substance. The World Health Organisation (WHO) classifies endosulfan in Category II (moderately hazardous). The US Environmental Protection Agency (US EPA) classifies it as a Category 1b (highly hazardous) pesticide[3]. Short-term toxicity is high, and influenced by the solvents and emulsifiers used to dissolve it[4]. Endosulfan is easily absorbed by the stomach, by the lungs and through the skin, meaning that all routes of exposure can pose a hazard[5]. Exposure to endosulfan may result from, for example: breathing air near where it has been sprayed; drinking water contaminated with it; eating contaminated food; touching contaminated soil; smoking cigarettes made from tobacco with endosulfan residues; or working in an industry where endosulfan is used[6]. Proper protective clothing (safety goggles, gloves, long sleeves, long pants, respirator) is needed to prevent poisoning when handling endosulfan[7].

Acute toxicity

Stimulation of the Central Nervous System is the main characteristic of endosulfan poisoning. Symptoms of acute exposure include hyperactivity, tremors, decreased respiration, salivation, anaemia[8], and also unco-ordination and a loss of ability to stand[9]. Other signs of poisoning include gagging, vomiting, diarrhoea, agitation, convulsions and loss of consciousness. Blindness has been observed in cows, sheep and pigs which have grazed in fields sprayed with the compound[10]. People with diets low in protein may be more sensitive to the effects of this pesticide[11].

Chronic effects

Although the short-term toxicity of endosulfan is of immediate concern, there are also long-term effects to consider. Animal studies have shown effects on the kidneys, developing foetus, and liver from longer-term exposure to low levels of endosulfan. The ability of animals to fight infection was also lowered[12]. Organochlorine compounds, including DDT, PCBs and endosulfan, may be part of the cause for the decrease in the quality of semen, in increase in testicular and prostate cancer, an increase in defects in male sex organs, and increased incidence of breast cancer which has been observed in the last 50 years. Endosulfan has also been found to cause mutations[13].

Environmental fate

As for the environmental effects of endosulfan use, the compound has adverse effects on aquatic systems, and is highly toxic to fish, birds, fowl, bees and wildlife[14]. According to other sources[15,16] however, endosulfan is relatively non-toxic to beneficial insects such as parasitic wasps, ladybirds and some mites.

Endosulfan has only a moderate potential for bioaccumulation[17]. It breaks down much faster than the other organochlorines[18], and it leaves the body fairly quickly[19]. Despite its rapid degradation in water, endosulfan can persist for a relatively long period when bound to soil particles, which can be a source of later contamination[20]. The advantage is that there is no threat of leaching to groundwater, but the disadvantage is that endosulfan may be particularly prone to run-off immediately after spraying. 'Adequate management of soil and water on cotton farms is required to prevent transport off-farm to minimise this threat.' [21].

The half-life of endosulfan in water and in most fruits and vegetables is reported to be three to seven days[22]. However, half-life in sandy loam is reported to be between 60 and 800 days[23]. The degradation rate is dependent on the pH of the soil: alkaline conditions favour degradation, whereas acidic conditions slow down the process[24,25]. Adding endosulfan to soil appears to reduce the rate of degradation of other organochlorine pesticides already present in the soil, either because endosulfan reduces the populations of micro-organisms, or because of reduction of the activity of micro-organisms responsible for degradation of the other organochlorines[26].

Breakdown product

A big drawback with endosulfan is that the breakdown product, endosulfan sulphate, is more persistent than the parent compound, accounting for 90% of the residue in 11 weeks. Sulphate formation increases as temperatures increase[27]. In Australia significant amounts of endosulfan sulphate were observed in soil prior to spraying as residue from applications in previous seasons[28].

The regulatory status of endosulfan differs from one country to another, but a lot of countries have found it relevant to put in place specific regulation on endosulfan use, by banning, restricting, or severely restricting it. Endosulfan has been banned in at least the following countries: Denmark, Germany, Netherlands, Sweden[29], Belize and Singapore[30], and the Brazilian state of Rondonia[31]. Colombia[32] and Indonesia[33] were preparing for a ban on endosulfan. Its use is not allowed either in rice fields in Bangladesh, Indonesia, Korea and Thailand. Use is restricted or severely restricted in: Canada, Finland, Great Britain, Kuwait, the Philippines, Russia, Sri Lanka and Thailand[34] and in Madagascar[35]. Campaigns have been going on world-wide for several years to ban endosulfan completely[36,37].

Bed bugs – least toxic control

Bed bugs infesting a house give off a nasty smell from 'stink glands'. In these conditions, writes ***David Allen,*** *the only solution may be to throw out the old mattress and take practical steps which avoid toxic chemicals.*

There are 74 bug species belonging to the Cimicidae family that are known to feed on humans – the most frequently found being *Cimex lectularius* the common bed bug. Although they are not such a common nuisance today, bed bugs can still affect any household and are generally associated with low levels of hygiene and overcrowding. Other species such as the pigeon bug (*Cimex columbarius*) and the martin bug (*Oeciacus hirundinis*) found in martins' nests predominantly feed on birds but can also feed on human blood.

Biology

Bed bugs are wingless insects and as such move around by crawling or riding from place to place in clothing, luggage or other such transport. Distribution can be further exacerbated in places such as theatres and public transport, with infestations frequently occurring in hotels and other buildings where there is a high density and turnover of individuals.

Bed bugs are mostly found in bedrooms as they generally feed at night when the host is asleep. When not feeding they live in the bed frame or cracks and crevices around the room. They do not harbour in the mattress or bedding material. They are reddish brown in colour turning blood red after feeding. The adult reaches approximately 5mm in length and passes through five nymph stages over a period of time to 128 days. The female lays her eggs in batches of 10 to 50, they are white in colour and deposited on various surfaces with a thin glue. They take on average 10 days to hatch and can mature into adults within one to two months given ample food. The female is then ready to start laying eggs. The speed of development depends on temperature and food availability. Surprisingly, bed bugs can live longer without food and can go without feeding for up to 140 days; the adult typically lives for about 10 months but can survive for a year or longer in cool buildings. This sensitivity to temperature means bed bugs will start to die if temperatures drop below 9°C or rise above 36°C. However, modern buildings have created ideal conditions for the bed bug with central heating and easy access to adjoining properties being commonplace.

Non-toxic control

Bed bug bites generally cause the victim irritation and can lead to sleepless nights, some pain and swelling, although some individuals experience next to no allergic reaction at all. Bed bugs do not transmit any known disease. The bites often leave a hard whitish swelling and evidence of a heavy infestation will be the unpleasant smell created by the bugs 'stink glands'. Further evidence of infestation is finding eggs, blood and faecal material on sheets and pillows. Strategies for ridding a bed bug infestation depend on which species is present. If it is a bat, pigeon or swallow bug then the source of the infestation may be a nearby nest or bat roost in the roof or under eaves. Removal of this source and blocking ways back into the house will help to prevent future infestations. However, it must be remembered that all species of bats are protected and it is an offence under the Wildlife and Countryside Act to remove or even block access to any bat roosting site. English Nature can give further advice on this issue.

For the common bed bug it is wise to check possible harbourages in cracks in the bed frame, around door and window frames, behind pictures, fittings and loose wallpaper and in light fittings. Any holes, cracks or crevices must be washed to eliminate any eggs or waste that has accumulated and then caulked, painted or sealed. Bed bugs can easily climb surfaces like wood so to prevent them from gaining access to a sleeping host, barriers can be put in their way. Examples of this are the use of petroleum jelly on the legs of the bed, putting the legs inside smooth metal jars and moving the bed away from any surfaces such as walls. Mattresses should either be replaced or steam-cleaned and bedding washed at a high temperature, making sure to transport bedding in an enclosed plastic bag to stop contamination of other areas. Exposure to hot and cold temperatures is a useful part of an infestation reduction policy, and raising temperatures to between 36°C and 37°C for an hour or so will probably eliminate an infestation, and prolonged exposure to temperatures of 0°C to 9°C will also kill off adults in a matter of hours.

Chemical control

Chemical control strategies often start by flushing bed bugs out from their hiding places by use of a natural or synthetic pyrethroid based aerosol spray. This is then followed by use of other insecticides inside the premises, including the treatment of beds and other furniture. Active ingredients approved for use against bed bugs in the UK under the Control of Pesticides Regulations 1986 (COPR) are the following organophosphates: chlorpyrifos methyl, diazinon, fenitrothion, iodofenphos, pirimiphos-methyl and trichlorfon; and carbamates, bendiocarb and propoxur. These groups of chemicals act as nerve poisons which kill by inhibiting the nerve enzymne cholinesterase which disrupts the nervous system. More than half of these actives will have their licences revoked as part of the UK Health and Safety Executive (HSE) review of all anticholinesterase compounds. This process began in September 1998 when data call-in letters were sent to approval holders. Because of lack of support the following substances chlorpyrifos-methyl, diazinon (which shows evidence of mutagenicity and evidence of embryotoxicity), iodofenphos, trichlofon and propoxur (a suspected human carcinogen) have had their licences revoked[1,2].

The synthetic pyrethroids alpha cypermethrin, bioallethrin, bioresmethrin, cypermethrin, deltamethrin, d-phenothrin, permethrin, resmethrin, s-bioallethrin, tetramethrin and the OPs trichlorphon and fenitrothion are suspected of being endocrine disruptors. Endocrine disrupting chemicals may affect the balance of normal hormonal function of animals and are suspected of contributing to the decrease in male fertility, female reproductive problems, increases in prostate and breast cancer, and behavioural and developmental problems in children[3]. The German Federal Environment Agency suspects deltamethrin of affecting sperm and the placenta and dimethoate of affecting sperm and prolonging pregnancy[4].

The botanicals registered for use in the UK (pyrethrins and pyrethrum extract) are the only pesticides that are not suspected endocrine disruptors or anticholinestease compounds.

Comment

If the physical control techniques outlined above are followed then the use of pesticides should prove unnecessary. Recent reports of bed bug resistance to certain groups of active ingredients underlines the importance of non-toxic methods. Pest Control Operators will usually try a product from another group of actives until the problem is solved or they have run out of options[5]. Most of these chemicals are skin and eye irritants so use of them could replace one itch with another and the presence of pesticides in the bedroom, often on the bed and mattress is not advisable.

The main sources for this article were:

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3. Environmental endocrine disruptors, A handbook of property data, Keith, L. H., John Wiley and Sons, Inc., 1997, 1232pp.
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Fipronil

Fipronil is an insecticide discovered and developed by Rhône-Poulenc between 1985-87 and placed on the market in 1993. Although effective against a variety of pests, there are concerns about its environmental and human health effects. Actively marketed in many industrialised and developing countries its, worldwide use is increasing.

Fipronil is a member of the phenyl pyrazole class of pesticides, which are principally chemicals with a herbicidal effect[1]. Fipronil, however, acts as an insecticide with contact and stomach action. It is sparingly soluble in water[2]; is stable at normal temperatures for one year but not stable in the presence of metal ions and is degraded by sunlight to produce a variety of metabolites one of which (fipronil-desulfinyl (MB 46513)) is extremely stable and is more toxic than the parent compound[3].

Production

In 1997, production was around 480 tonnes per annum, and was expected to rise to 800 tonnes by 2000[4]. Production takes place at the Rhône-Poulenc Biochimie plant at Saint-Aubin-Lès-Elbeuf, France[5], but approval has recently been gained for another production plant in China which will ensure the synthesis, formulation and distribution for the insecticide Regent in the Chinese market[6].

Usage

Between 1987 and 1996 fipronil was evaluated on more than 250 insect pests on 60 crops worldwide[7] and crop protection accounted for about 39% of total fipronil production in 1997[8].

Fipronil is marketed under the trade name Regent for use against major lepidopterous and orthopterous pests on a wide range of field and horticultural crops and against coleopterous larvae in soils[9]. It is also employed for cockroach and ant control[10] under the trade names Goliath and Nexa including in the US, where it is also used against pests of field corn, golf courses and commercial turf[11] (trade name Chipco Choice). It has been used under the trade name Adonis for locust control in Madagascar[12,13,14] and in Kazakhstan[15].

Fipronil also controls termite pests and was shown to be effective in field trials in Africa[16,17] and Australia[18]. It is marketed under the name Termidor[19].

In 1999, 400,000 hectares were treated with Regent. It became the leading imported product in the area of rice insecticides, the second biggest crop protection market after cotton in China[20].

Fipronil under the trade name Frontline or Top Spot is also used to control fleas, ticks and mites on domestic animals[21,22] and as a pour-on or dip for cattle to control ticks[23]. In the UK, provisional approval for five years has been granted for fipronil use as a public hygiene insecticide[24].

Mode of action

Fipronil is an extremely active molecule and is a potent disruptor of the insect central nervous system via the (-aminobutyric acid (GABA) regulated chloride channel[25]. Despite the fact that the GABA channel is important in nerve transmission in both vertebrate and invertebrate animals[26], and that fipronil does bind to the GABA receptor in vertebrates, the binding is 'less tight" which offers a degree of selectivity[27].

Environmental fate

Field persistence is low-moderate in water and soil (half-life 10-130 hours (h) in water and 45-530 h in soil) with three major degradates formed in soil – RPA 20076 (amide), MB46513 (fipronil-desulfinyl), and RPA 104615 and two major metabolites in water, including MB 45950 (sulfide). Under aerobic conditions in soil several metabolites have been identified, including RPA 200766 and MB 46136 (sulfone)[28].

Fipronil's half-life on treated vegetation has been determined at 3-7 months, depending on the substrate and the habitat where it is applied[29].

Laboratory studies show direct and indirect photolysis, volatilization, and hydrolysis as contributors to fipronil field dissipation[30]. Of the major degradates identified in laboratory studies, only two (MB 46136 and RPA 200766) were found in field studies at amounts greater than the limit of detection[31].

Fipronil residues tend to stay in the upper 15 cm of soil and exhibit low potential to leach to groundwater[32].

In aquatic environments, fipronil residues rapidly move from the water to the sediment with over 95% of the residues being found in or on the sediments within one week of application[33].

Metabolic studies showed that there was a potential for bioaccumulation of the photodegradate MB 46513 in fatty tissues[34].

Acute toxicity

Fipronil is classed as a WHO Class II moderately hazardous pesticide and has a rat acute oral LD_{50} (the dose required to kill half a population of lab animals) is 97 mg/kg[35]. It is less toxic to mammals than to some birds, fish and most invertebrates.

Fipronil has moderate acute toxicity by the oral and inhalation routes in rats. Dermal absorption in rats is less than 1% after 24 h and toxicity is considered to be low. In contrast, it is of moderate dermal toxicity to rabbits[36].

The photodegradate MB46513 appears to have a higher acute toxicity to mammals than fipronil itself by a factor of about 10[37].

Chronic effects

Fipronil is neurotoxic in both rats and dogs as shown in the acute and sub-chronic screening in the rat, developmental neurotoxicity and chronic carcinogenicity studies in the rat and in two chronic dog studies[38].

There has been a low incidence of severe skin reactions to Frontline Spray treatment, Top Spot for Cats and Top Spot for Dogs, mostly resulting in skin irritation and/or hair loss at the site of application. There is some suggestion that dogs are more severely affected than cats[39].

Fipronil is carcinogenic to rats at doses of 300 ppm in males (12.68 mg/kg/day) and females (16.75 mg/kg/day)[40], causing thyroid cancer related to disruption in the thyroid-pituitary status[41]. However fipronil was not carcinogenic to female mice when administered at doses of 30 ppm[42,43].

Fipronil is associated with reproductive effects in rats fed 95.4% fipronil continuously in the diet at 300 ppm based on clinical signs of toxicity, decreased litter size, decreased body weights, decrease in the percentage of animals mating, reduction in fertility index, reduced post-implantation survival and offspring postnatal survivability, and delay in physical development[44].

Human health

There have been very few studies undertaken with human subjects, although human cells have been used in some carcinogenicity studies in which no adverse effects were detected[45].

Fipronil has been classified as a Group C (Possible Human) Carcinogen based on an increase in thyroid follicular cell tumours in both sexes of the rat[46]. In contrast, thyroid tumours induced by fipronil in rats are not considered of relevance to human health in the UK[47].

Two Top Spot products were determined by the New York State Department of Environmental Conservation to pose no significant exposure risks to workers applying the product. However, concerns were raised about human exposure to Frontline spray treatment in 1996 leading to a denial of registration for the spray product. Commercial pet groomers and veterinarians were considered to be at risk from chronic exposure via inhalation and dermal absorption during the application of the spray, assuming that they may have to treat up to 20 large dogs per day[48].

Effects on wildlife

Laboratory toxicity tests

Fipronil is highly toxic to certain groups of gallinaceous birds (Acute LD_{50} for Bobwhite quail = 11.3 mg/kg), while being relatively innocuous to passerines (LD_{50} for field sparrow = 1120 mg/kg) and wildfowl ($LD_{50}$for Mallard duck > 2150 mg/kg)[49].

The LD_{50} of fipronil for the fringe-toed lizard *(Acanthodactylus dumerili)*

[Lacertidae] has been estimated at 30 µg a.i./g body weight in laboratory tests, indicating that it is highly toxic. Mortality was delayed and lizards died during the four weeks after treatment[50]. Locomotor activity, prey consumption and body weight remained significantly lower in lizards fed fipronil treated prey than in the control group for 2-4 weeks after treatment. Data on other lizard species is not available[51].

Toxicity of fipronil to fish varies with species. It is very highly toxic to bluegill sunfish (LC_{50} (Lethal Concentration) (96 h) = 85 µg/l), highly toxic to rainbow trout (LC_{50} (96 h) = 248 µg/l) and highly toxic to European carp (LC_{50} (96 h) = 430 µg/l)[52 53]. It is very highly toxic to one of the African tilapia (*Oreochromis niloticus*) (LC_{50} (96 h) = 42 µg/l)[54]. Fipronil affects larval growth in rainbow trout at concentrations greater than 0.0066 ppm[55].

Fipronil is also toxic to a wide range of aquatic invertebrates, very highly toxic to shrimps and other crustacea and very highly toxic to oysters[56 57].

Fipronil is highly toxic to bees[58] and termites[59]. It had the highest acute toxicity for the parasitoid *Bracon hebetor* [*Hymenoptera: Braconidae*] with an LC_{50} of 0.09 ng/cm≤, and the second highest Risk Quotient (RQ) of the seven insecticides tested by the FAO Locustox study[60]. It appears to reduce the longevity and fecundity of female braconid parasitoids and 'long term effects on reproduction are to be foreseen with fipronil'[61]. Fipronil was given the highest hazard ranking for beneficial tenebrionid beetles of six insecticides tested in the Locustox study[62]. It is virtually non-toxic to earthworms[63].

The metabolite MB 46136 is more toxic than the parent to avian species tested (very highly toxic to upland game birds and moderately toxic to waterfowl on an acute oral basis)[64]. The metabolite MB 46136 is more toxic than the parent to freshwater fish (6.3 times more toxic to rainbow trout and 3.3 times more toxic to bluegill sunfish). Metabolites MB 46136 and MB 45950 are more toxic than the parent to freshwater invertebrates (MB 46136 is 6.6 times more toxic and MB 45950 is 1.9 times more toxic)[65].

Field studies

Few studies of effects on wildlife have been carried out, but studies of the non-target impact from emergency applications of fipronil (Adonis 7,5) as barrier sprays for locust control in Madagascar showed adverse impacts of fipronil on termites (*Coarctotermes* spp.), which appear to be very severe and long-lived. There were also indications of adverse effects in the short-term on several other invertebrate groups, one species of lizard (*Mabuya elegans*) and several species of birds (including the Madagascar bee-eater)[66].

Non-target effects on some insects (predatory and detritivorous beetles, some parasitic wasps and bees) were also found in field trials of fipronil for desert locust control in Mauritania[67] and very low doses (0.6-2.0 g a.i./ha) used against grasshoppers in Niger caused impacts on non-target insects comparable with those found with other insecticides used in grasshopper control[68]. The implications of this for other wildlife and ecology of the habitat remain unknown but appear unlikely to be severe.

Grasshopper control in Siberia resulted in a greater impact on non-target invertebrate wildlife from fipronil than from chlorpyrifos[69].

Sustainable agriculture

There is conflicting evidence over the suitability of fipronil for use in Integrated Pest Management (IPM), which is generally recognised as a route towards more ecologically sustainable agriculture. Field study results range from good selectivity by fipronil for certain beneficial insects and lower toxicity than (the highly toxic) methyl parathion and endosulfan[70]; through slight and transitory decline in abundance of certain predators and parasitoids and little difference between fipronil and other insecticides[71 72 73]; to reductions in beneficial arthropods and poorer crop damage prevention than a comparative insecticide[74].

Trials in Vietnam have suggested that fipronil use is incompatible with IPM in rice due to disruption of natural enemies and adverse effects on aquatic organisms[75 76]. The study also questioned whether fipronil acted as a stimulant to plant growth[77]. This finding and the effects on aquatic organisms were disputed by the manufacturers[78], but the disruption of natural enemies was not.

The Locustox study concluded that fipronil is relatively toxic to the beneficial invertebrates tested (natural enemies and soil insects)[79].

There are also potentially negative impacts for sustainable agricultural practices in rangeland in Madagascar from fipronil use in locust control, if reduced termite activity affects soil nutrient cycling and water infiltration into soil. However, further study would be necessary to confirm this possibility[80].

Developing country problems

There are few issues unique to fipronil in relation to its use in developing countries – most are relevant to all pesticide use. However, the following risks are noted in relation to fipronil because of its specific characteristics and the conditions and situations under which it may be used in less developed nations:

Climate – due to heat levels frequently encountered in the tropics, the likelihood of non-use of suitable protective clothing when applying fipronil or coming in contact with it shortly after application is increased. Due to possible human health hazards and known irritant characteristics of certain formulations, this is an area of concern.

Container disposal – pesticide containers become attractive and valuable assets in materially poor communities and are frequently taken for use as storage vessels, etc. They are rarely adequately cleaned beforehand. Due to possible human health hazards, this is an area of concern.

Illiteracy – problems associated with inability to read label warnings during use may lead to increased human health risks.

Poor ecological knowledge – where little is known of the ecology of habitats likely to be treated with fipronil, predictions cannot be made for effects on wildlife nor the implications for the structure and functioning of the ecosystem.

Unique, unusual and/or poorly known fauna – the wide differences in toxicity of fipronil to different (even closely related) animals means that risk assessment for areas with unusual fauna cannot be predicted without extensive studies on locally occurring species. The need for incorporation of data on indigenous species in risk assessment in semi-arid regions, especially temporary ponds has been emphasised[81 82].

Conclusion

Fipronil is a highly effective, broad spectrum insecticide with potential value for control of a wide range of crop, public hygiene, amenity and veterinary pests. It can generally be applied at low to very low dose rates to achieve effective pest control.

Questions have been raised about fipronil's suitability for use in IPM and studies suggest that this must be evaluated on a case by case basis. In certain situations it may disrupt natural enemy populations, depending on the groups and species involved and the timing of application.

Its acute toxicity varies widely even in animals within the same groups (see above). This means that the toxicological findings from results on standard test animals are not necessarily applicable to animals in the wild. Testing on local species seems particularly important in determining suitability of fipronil based products for registration in different countries or habitats and the likely risk to non-target wildlife.

Fipronil use requires careful consideration where contamination of the aquatic environment is likely, due to its high toxicity to some fish and aquatic invertebrates.

The dose levels at which fipronil produces thyroid cancer in rats are very high and unlikely to occur in normal conditions of use. There is also dispute as to whether this is relevant to human health risk. However, in developing countries where illiteracy, lack of protective clothing and use of insecticide drums increase the risk of human contact with the product at above recommended dose rates, a precautionary approach may be warranted.

In general, it would appear unwise to use fipronil-based insecticide without environmental monitoring to accompany its use, in situations, regions or countries where it has not been used before and where its use may lead to its introduction into the wider environment or bring it into contact with people.

The fact sheet was written by staff at the Natural Resources Institute. An expanded version is available in a Fipronil Briefing Document from PAN UK.

Trifluralin

Trifluralin is a widely used herbicide which is a suspected carcinogen. In some countries its use is increasing, while in other countries it is banned for its persistence and its threat to ecosystems.

Trifluralin is a selective, pre-sowing or pre-emergence herbicide used to control many annual grasses and broadleaf weeds in a large variety of arable and horticultural crops[1]. One of the dinitroanaline herbicides, trifluralin prevents weed growth by inhibiting root development through the interruption of mitosis[2] – early developmental cell division. Trifluralin is applied as a soil-incorporated pesticide, though there are also some surface uses[3].

Production

Trifluralin was first registered in the US in 1963[4]. Patented by Eli Lilly, and still produced by Dow (which took over Eli Lilly), among 24 producers[5]. Annual worldwide sales in 1998 were worth US$300 million, and 24,000 tonnes were produced[6].

Trifluralin is registered in more than 50 countries for use on more than 80 crop, vegetable and ornamental uses. The US remains the major current market, where trifluralin ranks as one of the five top-selling herbicides[7], and it is also widely used on cotton and other crops in Africa and other developing countries.

Use

The use of trifluralin is increasing rapidly in the UK in both the volume applied and the area treated. From 1996 to 1998, its use increased by 57% by area treated. From 1996 to 1999, the annual average weight applied totalled 659,904 kilograms. Trifluralin is the eighth most heavily used pesticide on all arable crops: in 1998 it was applied to 736,886 hectares in the UK[8].

Demand in the US for dinitroaniline pesticides, predominantly trifluralin, however, declined an estimated 2.8% from 1993 to 1998[9]. In the US, the use of trifluralin on soybeans and cotton accounts for about 75% of overall use. It was the most widely used herbicide on upland cotton in 1998, where it was applied to 57% of the area surveyed[10].

Trifluralin is used on winter wheat and barley, set-aside (arable land temporarily taken out of cultivation), oil-seed rape, brassicas, carrots, lettuce, sugar beet, and beans[11]. It is also applied to outdoor bulbs and flowers, fodder crops, glasshouse crops, Christmas trees, herbaceous plants, soft fruit and vegetables[12]. In other countries it is used on cotton, soybean, sunflower, canola, turf, alfalfa, tomatoes and vines. Trifluralin is almost exclusively a single-application, ground-applied or soil-incorporated treatment[13].

Acute toxicity

Trifluralin is classified by the World Health Organisation as unlikely to present an acute hazard in normal use[14].

Although not noted as an acutely toxic pesticide to test animals, the toxicity of certain formulated products containing trifluralin may be more toxic than the technical material itself[15]. So, whereas the LD_{50} dose (the amount of the chemical lethal to one-half of experimental animals) is 10,000 milligrams per kilo (mg/kg) in rats, and greater than 2,000 mg/kg for dogs, rabbits and chickens, the oral LD_{50} for the product Treflan TR-10 in rats is more than 500 mg/kg[16].

Skin sensitisation (allergies) may occur in some individuals exposed to trifluralin. Inhalation may cause irritation of the lining of the mouth, throat or lungs. The solvent in emulsifiable concentrates of trifluralin may cause irritation to the skin. Most cases of poisoning result from the carrier or solvent in formulated trifluralin products, rather than from the trifluralin itself[17].

Company data states symptoms from inhaling the vapours can include headaches, dizziness and collapse; if ingested, trifluralin can cause nausea, cramps and vomiting, and it may be irritating to the eyes[18].

Chronic effects

Prolonged or repeated exposure to trifluralin may cause skin irritation[19]. Animal studies have shown consumption of trifluralin at high levels over a long period of time can cause liver and kidney damage[20].

Cancer

Trifluralin is classified by the US Environmental Protection Agency (EPA) as Group C, possible human carcinogen[21]. In a two-year study of rats fed 325 mg/kg per day, malignant tumours developed in the kidneys, bladder and thyroid[22]. Because there is a possible increase in the risk of cancer to humans, the EPA's Lifetime Health Advisory level for trifluralin in drinking water of 5 micrograms per litre includes an additional safety margin[23].

A concern about the carcinogenicity risk of occupational exposure to trifluralin is also acknowledged by the US EPA, with the stipulation that workers, particularly mixers, loaders, and applicators, should use personal protective equipment including coveralls, chemical-resistant gloves, shoes and socks. Post-application, workers should observe a 12 hour Restricted Entry Interval[24], a condition which is unlikely to be communicated or observed in developing countries.

Endocrine-disrupting effects

Trifluralin is an endocrine-disrupting chemical, according to both the UK Environment Agency and the World Wide Fund for Nature[25]. These chemicals have adverse, 'gender-bender' effects by interfering with the body's hormones, or chemical messengers, and are active at even miniscule levels (see PAN *UK* briefing No.2 *Mixed messages: pesticides that confuse hormones*).

Reproductive effects

Loss of appetite and weight loss followed by miscarriages were observed when pregnant rats were fed 224 or 500 mg/kg per day. Foetal weight decreased and there was an increase in the number of foetal runts at 500 mg/kg per day dosage[26].

Fate in the environment

The persistence of trifluralin in agricultural soils following incorporation is highly variable, depending on several factors including depth of incorporation, soil moisture and temperature. Its persistence is categorised as 'moderate' to 'persistent'[27]. Several field dissipation studies in northern latitudes in Canada indicated half-lives ranging from 126 to 190 days[28].

Trifluralin residues in the atmosphere of remote, non-use regions have been reported, suggesting its potential for long-range transport. Scientists found traces of trifluralin in the Canadian Arctic, which were believed to be from from Asia, probably China, in 1991[29].

Trifluralin pollutes the atmosphere and is carried long distances in dust and air. There is a general lack of understanding concerning mechanisms controlling the potential for such long distance transport. Further work is needed to understand the interactions and fate of trifluralin in the atmosphere[30].

Trifluralin is volatile, especially in wet conditions. A study found that when surface-applied to a wet fallow field, trifluralin losses through volatilisation range from 50% to 90% of the amount applied within a few hours or days[31].

Wildlife

Trifluralin is highly toxic to aquatic animals (fish and invertebrates) and it poses high risks to endangered species. Sediment-feeding organisms are particularly at risk because of the tendency of trifluralin to bioaccumulate. Studies also suggest exposure-related abnormalities in the vertebral development of aquatic animals, at low concentrations[32].

Food residues

Residues of trifluralin have been found to concentrate in peppermint oil and spearmint oil[33]. No UK or EU MRLs have been set. Trifluralin was found in UK carrots in the period 1991-99 but its use in this crop has since declined greatly[34].

Resistance

Resistance in blackgrass to dinitroanilines was first recorded in 1987 in the UK. Common British weeds now resistant to trifluralin include shepherd's needle, smooth sow-thistle, common couchgrass, creeping thistle and cleavers[35]. Weeds in US cotton crops are now commonly resistant to trifluralin[36].

Safety precautions

The manufacturers stipulate that containers which have had trifluralin in them should not be re-used[37]. A study to find out whether pesticide containers were safe to recycle found that trifluralin was the pesticide released in the highest quantities from recycled plastic[38].

Regulation

Trifluralin is currently under review as a priority substance under the European Commission's Water Framework Directive process[39], and is on the OSPAR 1998 list of candidate substances[40], comprising hazardous chemicals in the marine environment.

It was brought under Special Review in 1979 by the US EPA because of the presence of a N-nitrosamine contaminant which had been shown to cause tumours and to have mutagenic effects in animals. The review was concluded in 1982, with the requirement that this contaminant should not exceed 0.5 parts per million, a level which the EPA believes will have no toxic effects[41].

The only two products containing trifluralin were withdrawn from the Swedish market in 1990, because the chemical enters aquatic ecosystems under normal use conditions, and it was considered to pose an unacceptable risk to aquatic organisms due to effects at low concentrations and a high bioaccumulating potential; the substance is also persistent with a half-life of at least six months or longer[42]. The chemical was withdrawn from the Danish market in 1997, because fieldwork in four different soil-types showed its half-life was 201, 165, 143 and 289 days respectively; in Denmark pesticides with a half-life of more than three months cannot be registered[43]. Trifluralin is not authorised in the Netherlands[44] or in Norway, where it was banned in 1993[45].

Conclusions

It is a matter of concern that the use of the herbicide trifluralin, an endocrine-disrupting chemical and possible human carcinogen, is increasing significan ly in the UK. As there is evidence that the pesticide has chronic health effects, even at very low doses, its use in agriculture should concern regulators, public health professionals and the public.

The use of trifluralin is unsustainable because of growing resistance problems. As it is highly toxic to aquatic life, it could jeopardise vulnerable populations of protected species. Its known tendency to volatilise, and to travel great distances in the atmosphere, mean that trifluralin could become a widespread contaminant.

Herbicides such as trifluralin are used in increasing amounts against the pest problems created by monocultural agriculture. An alternative approach, which is not dependent on chemical pest control, builds soil fertility and uses crop rotations, creating natural resilience against pests. The uncontrolled dispersal of these chemicals in the environment imposes costs to human health, and to wildlife, which are unacceptably high. *(AC)*

Metaldehyde

Metaldehyde is used widely around the world as a molluscicide to kill slugs and snails, although it is toxic to all animals that ingest it. There is widespread concern that there has been an unacceptable number of poisoning incidents especially involving domestic pets, wild animals and birds.

Uses

Metaldehyde is applied as a molluscicide bait for controlling slugs and snails in a very wide range of agricultural and horticultural crops, and by members of the public to control slugs and snails in their gardens and allotments. In the UK, along with methiocarb (another slug and snail killer), metaldehyde is the only pesticide approved for use on all crops.

In many countries, there is little information on metaldehyde usage in the public domain. In the UK, only figures from the agricultural sector are recorded. Metaldehyde, the most commonly used molluscicide, was applied across 355,465 hectares in 1998. Molluscicides in general are applied to about 8% of the area of all arable crops, and are most extensively used on potatoes and oilseed rape[1].

Slug and snail damage is an increasing problem in the UK due to changes in agricultural practice, such as the cessation of stubble burning, and also because of the wet, moderate climate.

Toxicity

The World Health Organisation (WHO) classifies metaldehyde as a class II 'moderately hazardous' pesticide. The acute oral LD_{50} (the dose required to kill half a population of laboratory animals) for rats is 283 mg/kg[2].

Metaldehyde is highly toxic by inhalation, moderately toxic by ingestion and slightly toxic by dermal absorption. Skin and eye irritation may result from exposure to this material. Inhalation of vapours of metaldehyde may cause severe irritation of the mucus membranes lining of the mouth, throat, sinuses and lungs. Ingestion of metaldehyde causes irritation to the stomach and intestines, and can cause kidney and liver damage. One to three hours after ingestion the following symptoms may occur: severe abdominal pain, nausea, vomiting, diarrhoea, fever, convulsions, and coma. Other symptoms of acute exposure include increased heart rate, panting, asthma, depression, drowsiness, high blood pressure, inability to control release of urine and faeces, incoordination, muscle tremors, sweating, excessive salivation, tearing cyanosis, acidosis, stupor and unconsciousness[3].

The US Environmental Protection Agency classifies metaldehyde as a Restricted Use Pesticide because of its potential short-term and long-term effects on wildlife. All product labels must include the following statement on the front panel: 'this pesticide may be fatal to dogs or other pets if eaten. Keep pets out of treated areas'[4].

Poisoning cases

Metaldehyde is toxic to all organisms that ingest it, either directly or as a result of secondary poisoning from consuming poisoned prey. Poisoning results in the depression or excitement of the central nervous system[5]. Molluscs (slugs and snails) are poisoned either by absorption of poison through the skin or by ingestion. As a reaction to the poison molluscs overproduce mucous which causes dehydration and an inability to move, therefore remaining open to predation[6].

It is dangerous to game, wild birds and animals. Some products contain proprietary cat and dog deterrent in order to avoid poisoning of these domestic animals[7].

The Wildlife Incident Investigation Scheme (WIIS) recorded 17 metaldehyde poisoning incidents involving cats and dogs in 1998[8]. Hedgehogs are very likely to eat poisoned molluscs resulting in serious internal damage caused by secondary poisoning[9]. Symptoms of metaldehyde poisoning in domesticated and wild mammals include inability to stand, blindness, change in respiratory rate, excessive sweating and salivation, sudden death and seizures[10]. Autopsy results from metaldehyde poisoned dogs show congestion and haemorrhages in the liver, kidneys and heart[11].

Chronic effects

Long-term repeated skin exposure to metaldehyde can result in dermatitis (inflammation of the skin) in humans. Prolonged eye exposure can cause conjunctivitis. Two-year toxicity studies and three-year toxicity reproductive studies in experimental rats found liver enzyme activity and increased liver and ovary weight at 250mg/kg in the diet. Fifty percent of female rats given this dose showed paralysis[12].

Metaldehyde or its breakdown products may cause problems in the central nervous system through an unknown mechanism. The autopsy of a 2 1/2 -year-old boy, who lived 33 hours after ingesting one tablet of metaldehyde, had areas of collapse and congestion in the lungs, as well as cellular changes in the liver and the kidney[13].

Alternatives

A parasitic worm (known as a nematode) is used as a biological control agent in agriculture. In gardens, hand picking, beer traps, biological control and physical barriers are all effective if used as part of an integrated pest management system.

Hand picking should be carried out in the evening or early morning and can be significantly aided by erecting shelters for molluscs on the ground including; wood, metal sheeting and grapefruit shells. Beer traps can be made out of household items or more sophisticated versions, which safeguard beneficial insects, are available to buy at garden centres or hardware stores. Biological controls include taking measures to encourage natural predators such as hedgehogs and frogs[14].

Conclusion

Slugs and snails are an increasing pest problem both to agricultural production and in domestic gardens and allotments. The Pesticides Safety Directorate and the Health and Safety Executive should address the approved use of metaldehyde in both agricultural and domestic use with a view to restricting use and therefore reducing the risk of poisoning incidents. Restricted use in the US illustrates the unacceptable risk to wildlife posed by the use of metaldehyde.

Integrated pest management incorporating several non-chemical controls can help to keep pest numbers under control. Natural predators, such as birds, hedgehogs and frogs, should be encouraged to establish viable populations through careful habitat management. ***(AW)***

Rotenone

A recent study linking rotenone – a pesticide with a 'natural' image, commonly used in organic farming and gardening – to Parkinson's disease, has increased demand for a level playing field in the safety assessment of pesticides. The current regulatory system, designed for synthetic agrochemicals, impedes research into, and registration of, least toxic, relatively benign pest control substances.

What is rotenone

Rotenone is a naturally occurring chemical with insecticidal, acaricidal[1] (mite and spider-killing) and piscicidal (fish-killing) properties, obtained from the roots of several tropical and subtropical plant species belonging to the genus *Lonchocarpus* or *Derris*. It is a selective, non-specific insecticide, used in home gardens for insect control, for lice and tick control on pets, and for fish eradications as part of water body management[2]. Both a contact and stomach poison to insects, it kills them slowly, but causes them to stop their feeding almost immediately[3]. It exerts its toxic action by acting as a general inhibitor of cellular respiration[4].

Production

Rotenoids, the rotenone-related materials, have been used as crop insecticides since 1848, when they were applied to plants to control leaf-eating caterpillars. However, they have been used for centuries (at least since 1649) in South America to paralyse fish, causing them to surface[5]. *Derris* root has long been used as a fish poison and its insecticidal properties were known to the Chinese well before it was isolated by E. Geoffrey in 1895[6]. The use of the ground root of certain species of *Derris* was patented in 1912, since when it has been established that the active compounds are rotenoids, of which the main insecticide is rotenone[7].

Rotenone is sold in dispersible powder, emulsifiable concentrate, and wettable powder formulations[8]. In the UK, two professional products are registered: Devcol Liquid Derris, and Liquid Derris, and nine amateur products, including two wasp-killers. Another product marketed by pbi contains a mixture of rotenone and sulphur, both a fungicide and insecticide[9].

Products containing rotenone are registered in Denmark, Ireland, UK, France, Spain, Italy[10]. One product for fisheries management is also approved in Sweden, for restricted use[11].

Use

In the UK, rotenone products are approved for use against aphids on flowers, ornamentals, protected crops, soft fruit, top fruit, and vegetables, and against sawflies in gooseberries, and slug sawflies in pears and roses[12].

Very little rotenone is used in commercial fruit and vegetable production in the UK. The average annual total – all crops – is just three kilograms, used to treat 93 hectares. Since 1983, the minimum area treated annually was 22 hectares in 1985/86, and the maximum was 165 hectares in 1991[13]. No data is collected for amateur usage, and total stocks for amateur products (in garden sheds and amongst wholesalers and retailers) are likely to be considerably greater than for professional use.

Other target organisms of rotenone include maggots, bagworms, codling moths, Japanese beetles, leaf hoppers, Mexican bean beetles, cabbage worms, thrips, stinkbugs, flea beetles, and vegetable weevils[14].

The UK Environment Agency, responsible for granting licences for the use of noxious substances for the taking or destroying of fish, under the Salmon and Freshwater Fisheries Act 1975, and rotenone is by far the most common chemical used for this purpose[15].

Use of rotenone in organic production

In organic production, the use of rotenone is permitted as an insecticide under European Union Regulation 2092/91, amended by 1488/97, Annex II (B)[16]. In response to a recent study linking rotenone to Parkinson's Disease[17], the UK Soil Association put a temporary ban on its use, pending further investigations.

Acute toxicity

Rotenone is classified by the World Health Organisation as a moderately hazardous, Class II[18]. The LD_{50} for rats (the amount of the chemical lethal to one-half of experimental animals) is between 132 and 1,500 mg per kilogram[19]. One factor in this wide variation may be the differences in the plant extracts used[20].

The acute oral toxicity of rotenone is moderate for mammals, but there is a wide variation between species[21]. It is less toxic for the mouse and hamster than for the rat; the pig seems to be especially sensitive. Recent studies have shown that in rats, rotenone is more toxic for females than males. It is highly irritating to the skin in rabbits[22], and to the eyes. In rats and dogs exposed to rotenone in dust form, the inhalation fatal dose was uniformly smaller than the oral fatal dose[23].

Rotenone is believed to be moderately toxic to humans with an oral lethal dose estimated from 300 to 500 mg/kg[24]. A lowest lethal dose of 143 mg/kg has been cited in a child[25]. Clinical experience seems to indicate that children, in particular, are rather sensitive to the acute effects of rotenone[26].

Human fatalities are rare, perhaps because rotenone is usually sold in low concentrations (one to five per cent formulation), and because its irritating action causes prompt vomiting. If the dust particle size is very small, and can enter deep regions of the lungs, rotenone's toxicity when inhaled may be increased. Acute local effects include conjunctivitis, dermatitis, sore throat, congestion, and vomiting. Inhalation of high doses can cause increased respiration followed by depression and convulsions[27]. On the basis of rabbit studies, absorption through the intact skin is low[28].

Chronic effects

Studies on dogs at high doses produced adverse changes in blood chemistry[29]. In dogs fed rotenone at 10 mg/kg per day for six months, weight loss and haematological effects were found. A No Observed Adverse Effect Level (NOAEL) of 0.4 mg/kg per day has been determined for rats (2-year study), and dogs (16-month study)[30].

Cancer

Published studies on the carcinogenic potential of rotenone are conflicting and inconclusive. Significant increases in mammary tumours have been reported in albino rats with intraperitoneal doses of 1.7 mg/kg/day for 42 days. But no evidence of carcinogenic activity was seen in hamsters at oral doses as high as 120 mg/kg/day for a period of 18 months[31].

Endocrine-disrupting effects

Rotenone is not included on any existing lists as an endocrine-disrupting pesticide[32].

Reproductive effects

Reproductive effects seem unlikely in humans at expected exposures. Foetotoxicity and failure of offspring are reported in guinea pigs at doses of 4.5 and 9.0 mg/kg/day for an unspecified period[33].

Teratogenic effects

Evidence for this is inconclusive. In one study, pregnant rats fed 5 mg/kg/day produced a significant number of young with skeletal deformities[34].

Neurotoxicity

The recent study administered rotenone by continuous infusion into the ugular vein of rats at dose levels of 1 to 12 mg/kg/body weight per day. The aim of the work was to develop a model for Parkinson's disease, rather than study the toxicity of rotenone, and why this chemical was chosen is not

clear. The optimal dose for producing Parkinson-like pathology was found to be 2 to 3 mg/kg/ body weight per day, clearly above the intravenous LD_{50}[35].

A subsequent study, using much lower levels of chemicals, found that a combination of paraquat and maneb, but neither one alone, creates in mice the exact pattern of brain damage seen in Parkinson's disease patients, and that older mice may be more sensitive to the combination than younger mice[36].

Consumer and occupational exposure

Estimates of operator exposures to rotenone products have been calculated. The Occupational Exposure Standard in air for rotenone is 5 mg/m^3 (8 hours), 10 mg/m^3 (10 minutes). For 'talc' (dust) it is 10 mg/m^3 (8 hours), respirable 1 mg/m^3 (8 hours)[37].

Fate in the environment

Rotenone is rapidly broken down in soil and water: its half-life in both is between one and three days[38]. Nearly all its toxicity is lost in five to six days of spring sunlight, or two to three days of summer sunlight. It does not readily leach from soil and it is not expected to be a groundwater pollutant[39].

Water

Rotenone is highly toxic to fish: most values for the 96 hour LC_{50} (lethal concentration required to kill half the test organisms) for different fish species and for daphnids (water fleas) lie in the range of 0.02 to 0.2 mg/litre. If used as a piscicide, it may also cause a temporary decrease in numbers of other aquatic organisms[40].

There is considerable controversy over the use of rotenone to kill non-game fish in water body management areas. One study found that the practice has a substantially harmful effect on biodiversity, in which several populations of the native fish showed negligible signs of recovering stocks, while populations of all exotic species are up[41].

Food residues

Rotenone is not included in regulatory food residue programmes, and therefore no data is available.

Data gaps

The data base supporting the approval of rotenone is not to current requirements. NOAELs have not been determined for repeated exposures, no information is available on the extent of studies on its effect on the brain, and there is insufficient data on genotoxicity.

Conclusion

PAN *UK* believes that the same precautionary principle should be applied to all pesticides, and that no substance, however long-term its use, should be assumed to be safe without scientific assessment. The problems evident for rotenone – insufficient usage data, inconclusive studies, concern about unknown synergistic activity with other substances, and potential health hazards, are consistent with problems found with the majority of registered agrochemicals. *(AC)*

Dimethoate

One of the most widely-used insecticides in the world, dimethoate is a particular concern to those exposed occupationally during manufacture, formulation and use. It is acutely toxic, has possible links to cancer and is suspected of causing birth defects.

Dimethoate is a widely used organophosphorus (OP) insecticide applied to kill mites and insects systemically and on contact[1]. It was introduced in the 1950s, originally patented by American Cyanamid[2], and is now produced by 39 companies around the world[3]. Dimethoate is used against a broad range of insects such as thrips, aphids, mites, and whiteflies[4], and on a number of crops including citrus, cotton, fruit, olives, potatoes, tea, tobacco and vegetables[5]. It is also permitted for the control of the flies in livestock accommodation[6], home gardens and food storage[7]. Like all OPs, dimethoate acts by interfering with the activities of cholinesterase, an enzyme essential for the proper functioning of the nervous system of insects and humans[8].

Production and use

Dimethoate is used in a large number of products. In the US, it has 166 approved labels[9]. Its trade names include Afidox (produced by Lucava), Cekutoate (Cequisa), Perfekthion (BASF), Rogor (Isagro), Dimezyl (Agriphar), Hilthioate (Hindustan), and Teeka (Nagarjuna Agrichem)[10]. The large number of producers and products reflect the fact that it is one of the most commonly used insecticides in agriculture. In 1998, there were 16,250 metric tonnes of sales globally, with a value of $US 180 million[11].

In 1993, dimethoate applications to orchard crops in the US accounted for 35% of the total active ingredient used in agricultural applications, totaling approximately 725,000 pounds (329,000 kg)[12]. Applications made to 10 crops accounted for more than 80% of the total dimethoate applied in the US during 1993. These crops included cotton (17.1%), alfalfa (15.4%), oranges (7.7%), wheat (7.0%), apples (6.9%), grapefruit (6.9%), lemons (6.4%), peas/beans (5.68%), lettuce (3.9%) and field maize (3.1%)[13].

In the UK, dimethoate use in 1998 was 377,030 spray hectares on arable crops[14], an increase from 291,578 treated hectares in 1996[15]. It is mostly used against aphids on wheat (322,883 spray hectares in 1998), making it the second most widely used insecticide in wheat (accounting for 14% of all insecticides used), and the 23rd most widely used active substance in UK agriculture in 1998[16].

Acute toxicity

Dimethoate is moderately toxic (World Health Organisation class II) by ingestion, inhalation and dermal absorption[17]. Most oral LD_{50}s (dose at which half the sample is dead) in rats range from 150-400 mg/kg body weight[18]. For mice, rabbits and guinea pigs, the LD_{50}s are 160, 300 and 350 mg/kg respectively[19]. As with all OPs, dimethoate is rapidly absorbed through the skin, and easily absorbed through the lungs[20].

The population as a whole is not generally subject to exposure to dimethoate from air, water or food[21]; however occupational exposure may occur during manufacture, formulation and use. This mainly occurs through inhalation and dermal absorption, although occupational exposure can occur by accident or as a result of incorrect handling[22].

Where humans are exposed to dimethoate, there are many effects: when inhaled, the first effects are usually respiratory and may include a bloody or runny nose, coughing, chest discomfort, difficult or short breath, and wheezing due to constriction or excess fluid in the bronchial tubes. Skin contact may cause skin sensitisation. Eye contact will cause pain, bleeding, tears, pupil constriction and blurred vision. Following exposure by any route, other systemic effects may begin within a few minutes or be delayed for up to 12 hours. These may include pallor, nausea, vomiting, diarrhoea, abdominal cramps, headache, dizziness, eye pain, and blurred vision. Severe poisoning will affect the central nervous system producing lack of coordination, slurred speech, loss of reflexes, weakness, fatigue, involuntary muscle contractions, twitching, tremors of the tongue or eyelids, and eventually paralysis of the body extremities and the respiratory muscles[23].

Chronic effects

In humans, repeated or prolonged exposure to OPs may result in the same effects as acute exposure, including the delayed symptoms. Other effects reported in workers repeatedly exposed include impaired memory and concentration, disorientation, severe depressions, irritability, confusion, headache, speech difficulties, delayed reaction times, nightmares, sleepwalking and drowsiness or insomnia[24].

Teratogenicity (birth defects)

Dimethoate is a suspected human teratogen[25]. It has been demonstrated as teratogenic in dogs and cats: for example, one study found that a dosage of 12 mg/kg/day given to pregnant cats increased the incidence of extra toes on kittens. The same dosage given to pregnant rats produced both birth defects related to bone formation, stunting and defects related to malfunction of the bladder[26]. These results contradict previous statements made, for example, the UK Advisory Committee on Pesticides (ACP) evaluation in 1993 concluded 'dimethoate was not overtly teratogenic in rats or rabbits'[27], and in 1988 the International Programme on Chemical Safety (IPCS) stated 'on the basis of available data on experimental animals, dimethoate is not considered to be a teratogen'[28]. In 1994, BASF rejected claims made in Chile of a link between unusually high levels of genetic defects among babies born in the fruit-growing region of Rancagua with the usage of the insecticide dimethoate. BASF denied there was any evidence to support the claim[29].

Reproductive effects

Dimethoate may affect reproduction: in a multiple generation study in mice, reproductive performance was impaired at high doses but only in the presence of marked cholinergic effects. In an inadequate mouse multigeneration study in 1965, there was no overt effect on reproductive capacity at dietary levels up to 50 ppm[30]. However, another study showed that dimethoate at 60 mg/litre drinking water did affect mating of five generations of mice tested[31].

Mutagenicity

There is no consensus on mutagenicity. In 1989, the WHO concluded that dimethoate was found to be mutagenic in a variety of *in vitro* and *in vivo* studies[32]. In contrast, the various mutagenicity studies reviewed during ACP evaluation indicated that dimethoate possesses mutagenic potential *in vitro*, but is not mutagenic *in vivo*[33]. One study found dimethoate to be mutagenic in a continuous four generation *in vivo* experiment[34], contradicting the previous statement, whilst the US Environmental Protection Agency stated there was positive mutagenicity associated with dimethoate[35].

Cancer

Dimethoate is classified as a possible human carcinogen by the US EPA, based on tumors in mice, the compound-related (no dose response) weak effect of combined spleen, skin and lymph tumors in male rats, and positive mutagenic activity associated with dimethoate[36]. The IPCS concluded in 1989 that the available data were inadequate to assess the carcinogenic potential of the compound. The ACP 1993 evaluation concluded that dimethoate was not carcinogenic in rats or mice[37], however, an increase in malignant tumours has been reported in rats given oral doses of five,15 or 30 mg/kg dimethoate for 511 to 627 days[38]. It seems there is a lack of data assessing the carcinogenic potential of dimethoate.

Effects on wildlife

The toxicity of dimethoate for aquatic organisms and birds is moderate to high[39]. One study found that it causes temporary rhythm alterations in some bird seed-eating species. Whilst these effects may not be fatal, they

may be critical for the birds' food-finding ability and in making them more vulnerable to predators[40]. Dimethoate has also been found to affect wood mice behaviour[41] and to cause jumping, erratic movement imbalance and death in fish[42].

Dimethoate is highly toxic to bees on an acute contact basis[43], particular concern has been expressed over this[44]. The LD_{50} (oral and topical) for bees is 0.1-0.2 µg/bee[45]. Products containing dimethoate warn not to apply to crops in open flower nor when flowering weeds are present[46].

Fate in the environment

Dimethoate is a mobile, yet relatively non-persistent OP insecticide. The primary route of dissipation appears to be microbially-mediated degradation in anaerobic (oxygen-rich) soil, particularly under moist conditions, with a half-life (time taken to degrade to half its initial strength) of 2.4 days[47]. The 1999 ACP review discussed its previous concerns over environmental fate and behaviour. They concluded that dimethoate was unlikely to leach because it is so rapidly degraded in soil, is non-volatile, was slightly persistent in sediment/water systems with a DT_{50} of 13-17 days and did not significantly partition to sediment[48].

Resistance

The peach potato aphid is known to be resistant to dimethoate in the UK. However, other aphid species and leaf miner do not exhibit such resistance[49].

The cocktail effect

It appears dimethoate creates a metabolite called demethoxon that plays a dominant role in the toxicity of dimethoate for insects and mammals. Dimethoxon is also used as an insecticide known as omethoate. Omethoate, is about 10 times more toxic and is more of a potential inhibitor to cholinesterase activity than dimethoate[50]. This is an important issue as, in the past, the intake of dimethoate and omethoate have been considered separately, and consumer exposure from individual crop uses has remained below the Acceptable Daily Intake (ADI). However, if the total diet is taken into account, the ADI could be exceeded for toddlers by both dimethoate and omethoate residues and for infants by dimethoate residues. The Pesticides Safety Directorate is in the UK is currently examining the issue of combined residues[51].

Conclusions

Unlike organochlorine pesticides, OPs such as dimethoate do not persist in the environment. Instead, their problem lies in their health effects on humans and other organisms. There is little concrete evidence regarding the chronic effects of dimethoate, for example on its carcinogenicity, however its acute effects on the nervous systems of humans and wildlife have been widely observed. Even though safer alternatives to OP insecticides are available, dimethoate still remains one of the most widely used insecticides in the world. Further safer alternatives should be developed, and an alternative approach based on the encouragement of natural pest enemies widely adopted. ***(HM)***

Source: pp 75-111 of this publication are drawn from various issues of Pesticides News published by Pesticide Action Network, UK, London (formerly The Pesticides Trust)

List of pesticides registered for use in the country

under section 9(3) of the Insecticides Act, 1968 (June 2002)

S.N.	Name	WHO Class
1.	2-4-Dichlorophenoxy Acetic Acid	II
2.	Acephate	III
3.	Acetamiprid	
4.	Alachlor	III
5.	Aldicarb	Ia
6.	Allethrin	III
7.	Alphacypermethrin	O
8.	Alphanapthyl Acetic Acid	
9.	Aluminium Phosphide	
10.	Anilophos	II
11.	Atrazine	U
12.	Aureofungin	
13.	Azadirachtin (Neem Products)	
14.	Bacillus thuringiensis	
15.	Barium Carbonate	III
16.	Benomyl	U
17.	Benthiocarb (thiobencarb)	II
18.	Bitertanol	U
19.	Bromadiolone	Ia
20.	Butachlor	U
21.	Captafol	Ia
22.	Captan	U
23.	Carbaryl	II
24.	Carbendazim	U
25.	Carbofuron	Ib
26.	Carbosulfan	II
27.	Carboxin	U
28.	Cartap Hydrochloride	U
29.	Chlorimuron ethyl	U
30.	Chlormequat Chloride	III
31.	Chlorobenzilate	III
32.	Chlorofenvinphos	Ib
33.	Chlorothalonil	U
34.	Chlorpyriphos	II
35.	Cinmethylene	U
36.	Copper Hydroxide	III
37.	Copper oxychloride	III
38.	Copper Sulphate	II
39.	Coumachlor	U
40.	Coumatetralyl	Ib
41.	Cuprous oxide	II
42.	Cyfluthrin	II
43.	Cyhalofop-butyl	U
44.	Cymoxanil	III
45.	Cypermethrin	II
46.	Cyphenothrin	II
47.	Dalapon	U
48.	Dazomet	III
49.	Decamethrin (Deltamethrin)	II
50.	Diazinon	II
51.	DDT	II
52.	Dichloropropene and Dichloropropane mixture (DD Mixture)	F
53.	Dichlofop Methyl	III
54.	Dichlorvos (DDVP)	Ib
55.	Dicotol	III
56.	Dieldrin	
57.	Difenoconazole	III
58.	Diflubenzuron	U
59.	Dimethoate	II
60.	Dinocap	III
61.	Diathianon	III
62.	Diuron	U
63.	Dodine	III
64.	D-trans Allethrin	
65.	Edifenphos	Ib
66.	Endosulfan	II
67.	Ethephon	U
68.	Ethion	II
69.	Ethofenprox (Etofenprox)	U
70.	Ethoxysulfuron	
71.	Ethyline Dobromide (EDB)	F
72.	Ethyline Dibromide and Carbon Tetrachloride mixture (EDCT mixture)	
73.	Fenarimol	U
74.	Fenazaquin	II
75.	Fenitrohion	II
76.	Fenobucarb	II
77.	Fenoxaprop-p-ethyl	U
78.	Fenopropathrin	II
79.	Fenthion	II
80.	Fenvalerate	II
81.	Ferbam	U
82.	Fipronil	II
83.	Fluchloratin	III
84.	Flufenoxyuron	U

S.N.	Name	WHO Class
85.	Fluvalinate	U
86.	Formothion	II
87.	Fosetyl-Al	U
88.	Gibberellic Acid	U
89.	Glufosinate Ammonium	III
90.	Glyphosate	U
91.	Hexaconazole	U
92.	Hydrogen Cynamide	F
93.	Imazethapyr	U
94.	Imidacloprid	II
95.	Indoxacarb	U
96.	Iprodine	
97.	Isoprothiolane	III
98.	Isoproturon	III
99.	Kasugamycin	U
100.	Kitazin (Probenfos)	III
101.	Lambdacyhalothrin	II
102.	Lime Sulphur	F
103.	Lindane	II
104.	Linuron	U
105.	Malathion	III
106.	Maleic Hydrazide (MH)	U
107.	Mancozeb	U
108.	Metafaxyl	III
109.	Metaldehyde	II
110	Metasulfuron Methyl	
111.	Methabenzthiazuron	U
112.	Methomyl	Ib
113.	Methoxyl Ethyl Mercury Chloride (MEMC)	U
114.	Methyl Bromide	F
115.	Methyl Chlorophenoxy Acetic Acid (MCPA)	III
116.	Methyl Parathion	Ia
117.	Metolachlor	III
118.	Metoxuron	U
119.	Metabuzin	U
120.	Monocrotophos	Ib
121.	Myclobutanil	III
122.	Nickel Chloride	F
123.	Oxadiargyl	
124.	Oxadiazon	U
125.	Oxycarboxin	U
126.	Oxydermeton-Methyl	Ib
127.	Oxyfluorten	U
128.	Paclobutrazole	III
129.	Paradichlorobenzene (PDCB)	III
130.	Paraquat dichloride	II

S.N.	Name	WHO Class
131.	Penconazole	U
132.	Pendimethalin	III
133.	Permethrin	II
134.	Phenthoate	II
135.	Phorate	Ia
136.	Phosalone	II
137.	Phosphamidon	Ia
138.	Propanil propanil	
139.	Prallethrin	II
140.	Pretilachlor	U
141.	Primiphos-methyl	III
142.	Profenophos	II
143.	Propanil	III
144.	Propetamphos	Ib
145.	Propiconazole	II
146.	Propineb	U
147.	Propoxur	II
148.	Pyrethrins (pyrethrum)	II
149.	Quinalphos	II
150.	Simazine	U
151.	Sirmate	
152.	Sodium Cyanide	Ib
153.	Spinosad	U
154.	Streptomycin+Tetracycline	
155.	Sulfosulfuron	
156.	Sulphur	U
157.	Tebuconazole	U
158.	Temephos	U
159.	Thiodicarb	II
160.	Thiomethoxin	
161.	Thiometon	Ib
162.	Thiophanate Methyl	U
163.	Thiram	III
164.	Transfluthrin	U
165.	Triadimefon	III
166.	Triallate	III
167.	Triazophos	Ib
168.	Trichloro Acetic Acid	II
169.	Trichlorofon	III
170.	Tricyclazole	II
171.	Tridemorph	II
172.	Trifluralin	U
173.	Validamycin	U
174.	Warfarin	Ib
175.	Zinc Phosphide	Ib
176.	Zineb	U
177.	Ziram	III

List of Pesticides Banned
(as on 17.06.02)

A. Pesticides Banned for manufacture, import and use (@$ Nos.)

1. Aldicarb
2. Aldrin
3. Benzene hexachloride
4. Calcium cyanide
5. Chlorbezilate
6. Chlordane
7. Copperacetoarsenate
8. Dibromochloropropane (DBCP)
9. Dieldrin
10. Endrin
11. Ethyl mercurychloride
12. Ethyl parathion
13. Ethylene dibromide (DBCP) use banned wef 17 .7.03
14. Heptachlor
15. Maleic hydrazide (banned wef 17.7.2003)
16. Menazon
17. Nitrofen
18. Paraquat dimethyl sulphate
19. Pentachlor nitrobenzene PCNB
20. Pentachlorophenol (PCP)
21. Sodium methane arsenate (MSMA)
22. Tetradifon
23. Toxafen
24. Trichloroacetic acid (banned wef 17.7.03)

B. List of Pesticide Formulations Banned

1. Carbofuran 50% G
2. Methomyl 12.5% L
3. Methomyl 24% L
4. Phosphaamidon 85% SL

C. Pesticides/Pesticide formulations banned for use but their manufacture is allowed for export

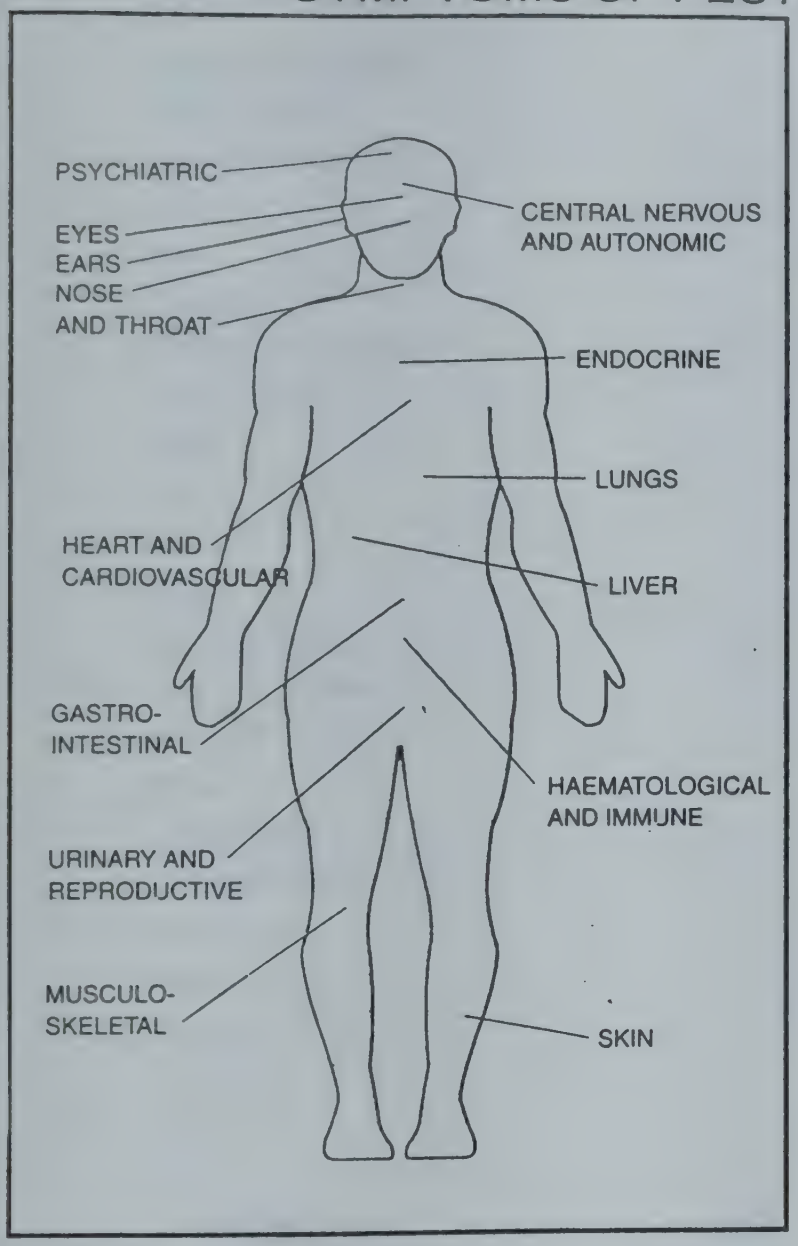
1. Captafol 80% (use banned wef 17.7.03)
2. Nicotin sulphate
3. Phenyl mercury acetate

D. List of Restricted Pesticides

1. Aluminium phosphide
2. DDT
3. Lindane
4. Methyl mide
5. Methyl parathion
6. Sodium cyanide
7. Thiram

A guide to pesticide exposure for physicians

SYMPTOMS OF PESTICIDE POISONING



HOW PESTICIDES GET INTO THE BODY

Pesticides may pollute: AIR, FOOD, WATER.

The commonest mode of entry is by direct contact with the skin, but they may also enter via the eyes, mouth (particularly in children) and lungs.

WHY PESTICIDES ARE TOXIC

Some are not broken down by nature's usual detoxification mechanisms.

They don't always stay where they are applied and can rapidly travel considerable distances.

The present safety levels are far too high. They take no notice of pre-existing illnesses and individual variation in metabolism.

Chronic low-level exposure to pesticides may cause bioaccumulation in body fat.

Interaction may occur between pesticides, when ingested, and existing drug therapy.

Some have to be used at concentrations that may be hazardous to humans unless adequate BPE or clothing is used.

ACUTE	CHRONIC
CENTRAL NERVOUS AND AUTONOMIC	
Exhaustion, weakness, paralysis, acute headache, nausea, vomiting, tremor, peripheral neuropathy, fever, blurred vision, contracted pupils, sweating, salivation.	Incoordination, fits, unsteadines numbness, tingling, acute depression, symptoms that mir recognised neurological dis-eases.
EYES EARS NOSE AND THROAT	
Burning, irritating and watering mucous membranes of eyes, ears, nose and throat.	Conjunctivitis, rhinitis, sore-throa and eye damage.
HEART AND CARDIOVASCULAR	
Slow pulse, cardiac arrythmias, heart block.	Chest pains, circulatory failure, heart muscular damage.
LUNGS	
Shortness of breath, bronchospasms, excess secretions, cyanosis, respiratory depression.	Asthma, burning and irritation, lung damage.
URINARY AND REPRODUCTIVE	
Dysuria, frequency of urination, uncontrollable incontinence, spontaneous abortion.	Kidney damage, sterility, foetus malformation.
MUSCULO-SKELETAL	
Muscle cramps, tremor, paralysis, muscular twitching.	Muscular tenderness, low muscle strength, muscle cramps.
SKIN	
Burning, itching.	Persistent dermatitis, especially of hands, eczema.
GASTRO-INTESTINAL	
Excessive thirst, nausea, vomiting, abdominal pains and cramps, diarrhoea, loss of sphincter control.	Odd taste in mouth, weight loss, bleeding internally.
LIVER	
Necrosis, some hepatic malfunction.	Disruption of enzyme systems; low tolerance to chemicals and alcohol, chemical hepatitis, jaundice.
ENDOCRINE	
	Suppression of adrenal cortex, hyperthyroidism, hyperglycaemia, suppression of endocrine function.
PSYCHIATRIC	
Irritability, loss of memory and concentration, anxiety.	Chronic fatigue, personality change, emotional problems, lassitude, depression, reduced drive, insomnia.
HAEMATOLOGICAL AND IMMUNE	
Immune system depression.	Anaemias, clotting problems, white cell depression.

Pesticide Poisoning Report Proforma

Place: जगह | **Date:** दिनांक | **Time:** समय

Name of patient affected:
नाम

Address:
पता

Age of the patient: उम्र | **Sex:** लिंग

Nature of symptoms:
रोग के लक्षण

Name of person who reported:
सूचना देने वाले व्यक्ति का नाम

Address:
पता

What was patient doing when affected?
रोगी घटना के समय क्या कर रहा था?

At home: घर में | **Factory:** फैक्ट्री | **Field:** खेत में | **Any other** अन्य

Name of product being used:
उत्पाद का नाम

Treatment given, if any:
यदि कोई उपचार दिया हो

Any other information:
अन्य जानकारी

Statement Showing the Number of Pesticide Poisoning Cases (Statewise) During 1996–99

S.No.	Name of States/UTs	1996-97	1997-98	1998-99
1.	Andaman & Nicobar	Nil	Nil	Nil
2.	Andhra Pradesh	13	Nil	76
3.	Arunachal Pradesh	N.R	Nil	Nil
4.	Assam	Nil	Nil	Nil
5.	Bihar	N.R	Nil	Nil
6.	Chandigarh	Nil	Nil	Nil
7.	Dadra & Nagar Haveli	N.R	N.R	N.R
8.	Daman & Diu	N.R	N.R	N.R
9.	Delhi	N.R	N.R	N.R
10.	Goa	Nil	Nil	Nil
11.	Gujarat	2	Nil	Nil
12.	Haryan	302	151	125
13.	Himachal Pradesh	N.R	N.R	55
14.	Jammu & Kashmir	N.R.	Nil	Nil
15.	Karnataka	Nil	5	Nil
16.	Kerala	803	834	648
17.	Lakshadweep	N.R	N.R	N.R
18.	Madhya Pradesh	Nil	Nil	Nil
19.	Maharashtra	815	2751	3358
20.	Manipur	Nil	Nil	Nil
21.	Meghalaya	Nil	Nil	Nil
22.	Mizoram	Nil	Nil	Nil
23.	Nagaland	Nil	Nil	Nil
24.	Orissa	Nil	Nil	Nil
25.	Pondicherry	549	415	291
26.	Punjab	180	252	586
27.	Rajasthan	418	420	421
28.	Sikkim	Nil	Nil	N.R
29.	Tamil Nadu	379	73	143
30.	Tripura	Nil	Nil	Nil
31.	Uttar Pradesh	Nil	42	Nil
32.	West Bengal	N.R	N.R	N.R

Remarks: The figures have been compiled based on the information furnished by the States/UTs either at the Zonal Conferences or figures furnished to Govt. of India, Ministry of Agriculture, Department of Agriculture & Cooperation, Directorate of Plant Protection, Quarantine & Storage, Faridabad.

"N.R" – Not Reported.

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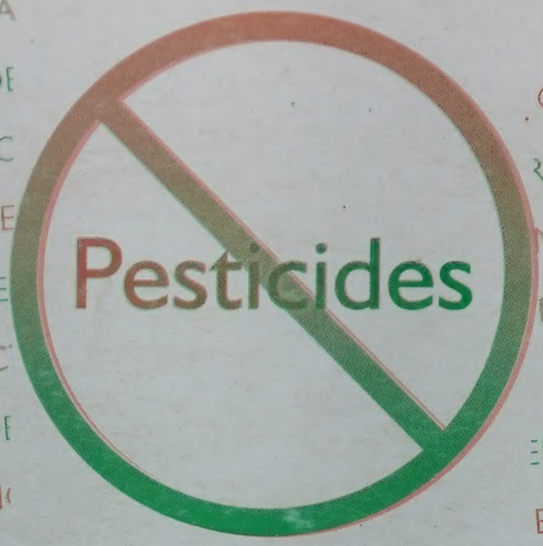
* Not part of the official Registered Pesticides. Included only as supplementary information.



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